Management of Heart Failure: Time to Consider New Options?

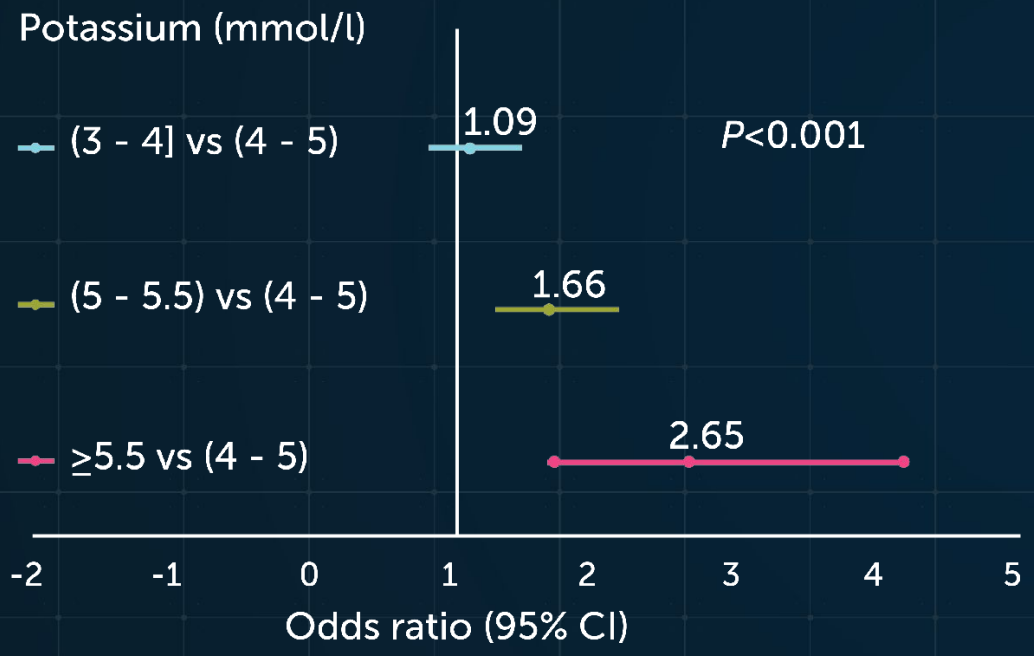
“Concerns and fears about hyperkalemia lead to suboptimal use of RAASi therapy which can negatively affect patient outcomes.”

Challenges with Potassium Management Options

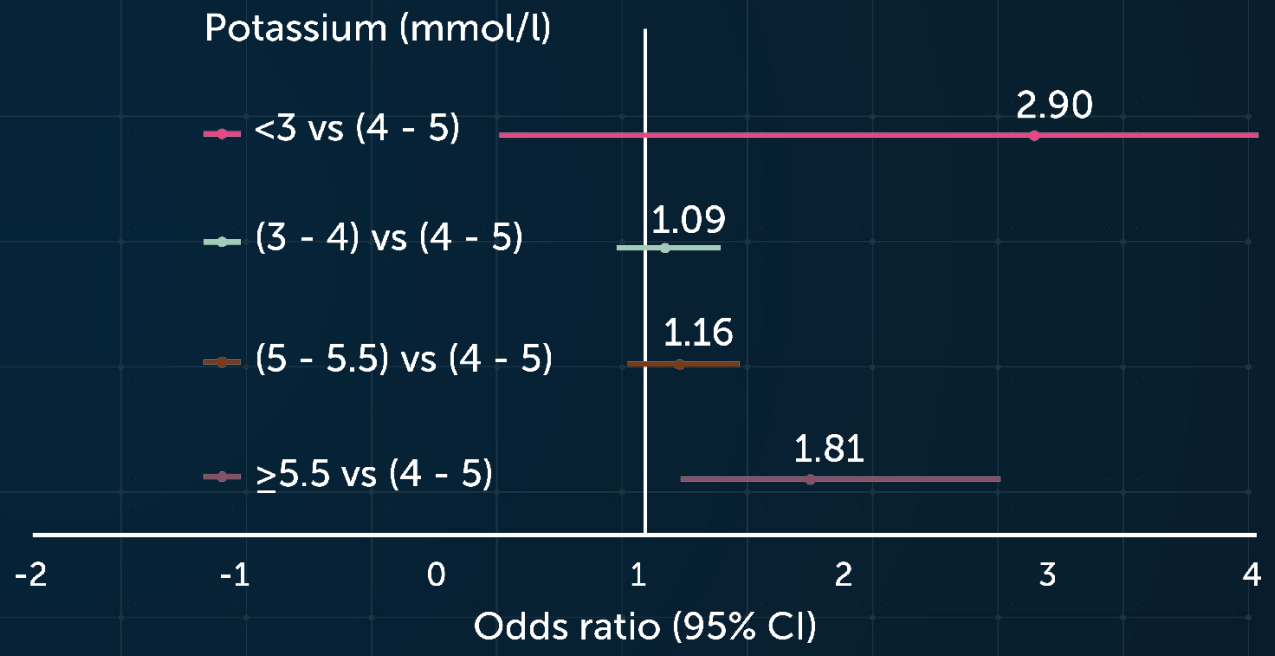
- Low-potassium diets
  - Adherence is difficult
- High-dose loop diuretics
  - Affects renal hemodynamics and increases counterregulatory hormones
- Sodium polystyrene sulfonate (SPS)
  - Not well tolerated
  - Rare but significant GI side effects
  - Potential for significant sodium load

GI = gastrointestinal

ESC-HFA-EORP Heart Failure Long-Term Registry



Predictors of Low Dosage MRA Usage



MRA Discontinuation During 1-year Follow-up

Rossignol P, et al. *Eur J Heart Fail*. Published online April 3, 2020. doi: 10.1002/ejhf.1793

European Society of Cardiology Consensus

- Use an approved potassium-lowering agent when K^+ >5 mmol/L to achieve guideline recommended target dose of RAASi therapy

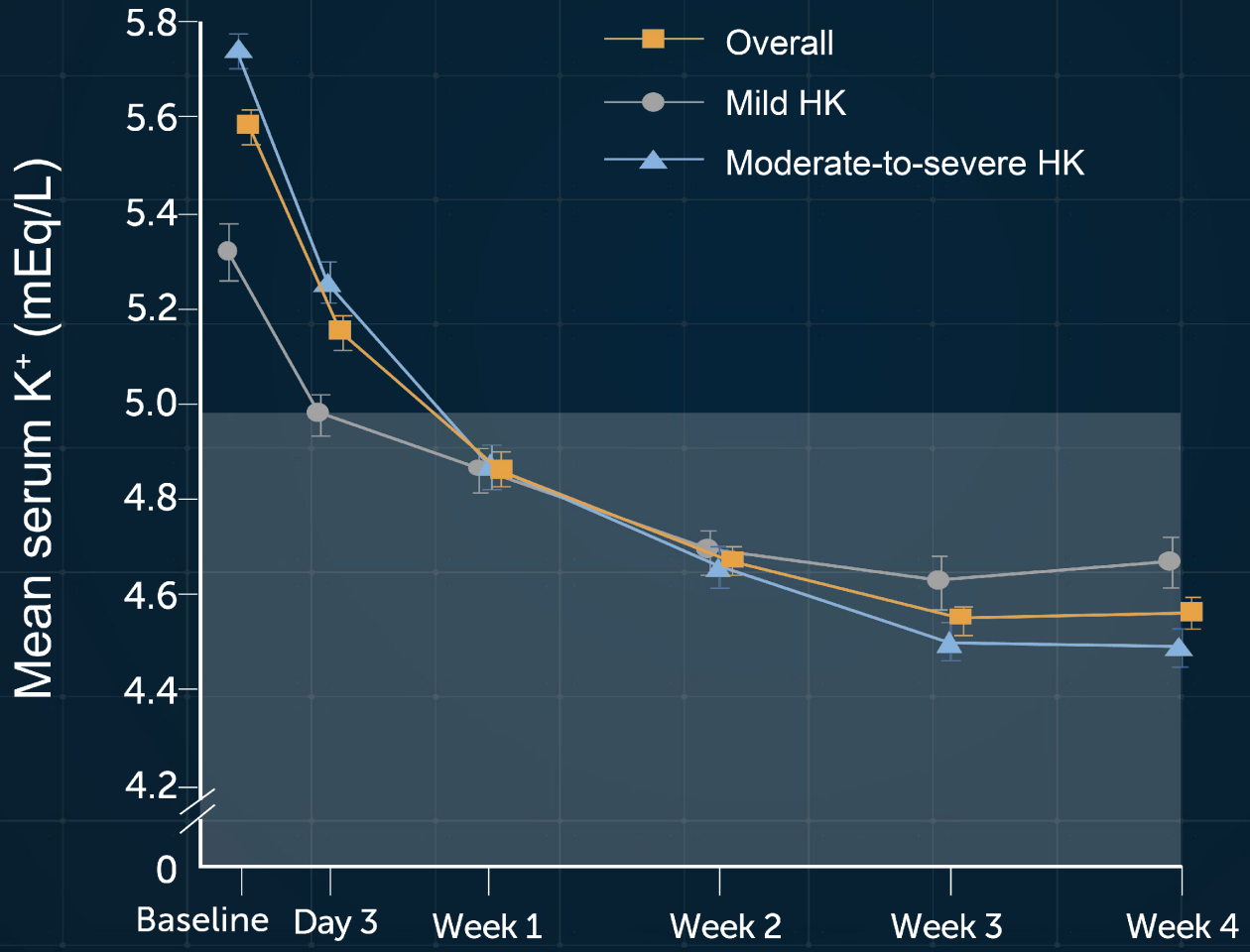
Rosano GMC, et al. *Eur Heart J Cardiovasc Pharmacother*. 2018;4(3):180-188.

Patiromer

- Exchange resin
- K^+ exchanged for Ca^{2+}
- Works in the distal colon

OPAL-HK: Patiromer Reduces Serum K^+

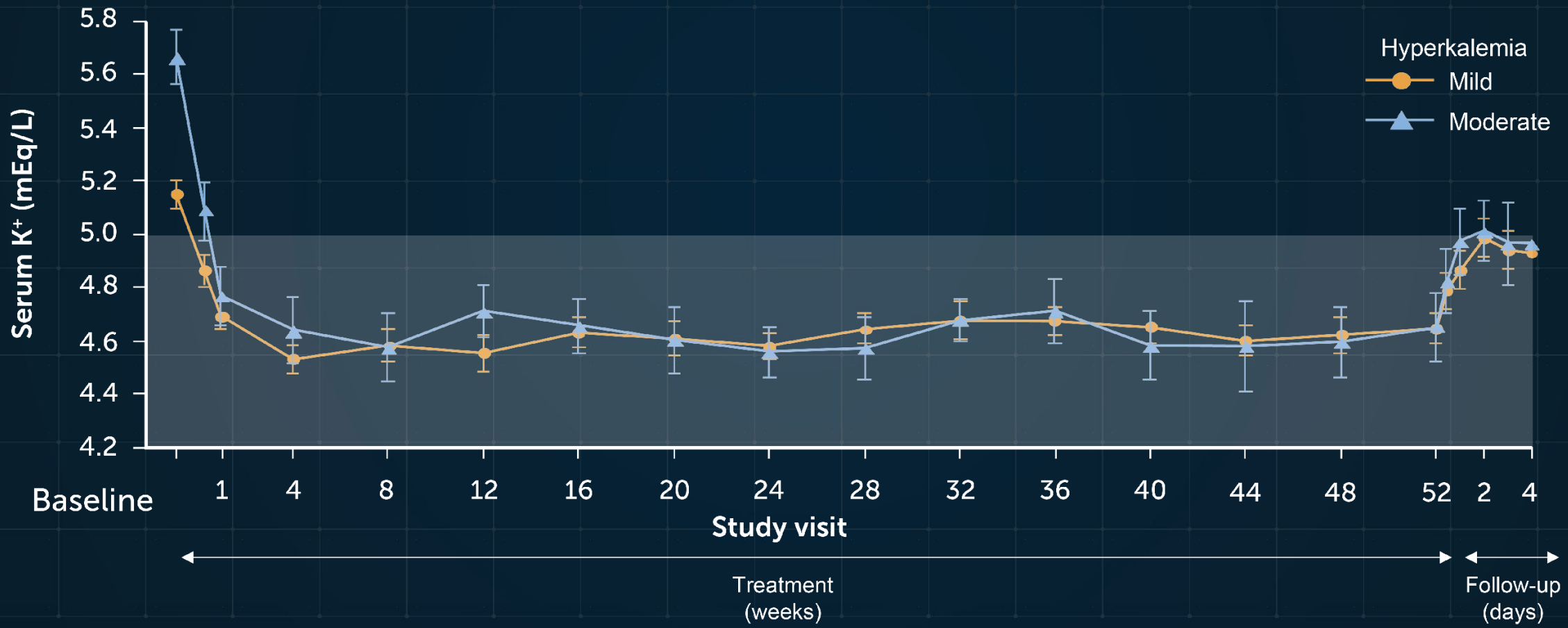
Patients with CKD stage 3/4 with hyperkalemia ($K^+ \geq 5.1$ mEq/L), using RAASi, N = 243



CKD = chronic kidney disease, RAASi = renin-angiotensin-aldosterone system inhibitor; Weir MR, et al. *N Engl J Med.* 2015;372(3):211–221.

AMETHYST-DN: Patiromer Maintains Normokalemia

Patients with CKD, T2DM, ± hypertension, hyperkalemia (K^+ >5.0 mEq/L), using RAASi, N = 306



CKD = chronic kidney disease, T2DM = type 2 diabetes mellitus, RAASi = renin-angiotensin-aldosterone system inhibitor

Bakris GL, et al. *JAMA.* 2015;314(2):151–161.

AMETHYST-DM: Patiromer Adverse Events

- Constipation 6.3%
- Diarrhea 5.6%
- Potentially better GI tolerability than SPS
- Hypokalemia 5.6%
- Hypomagnesemia 8.6%

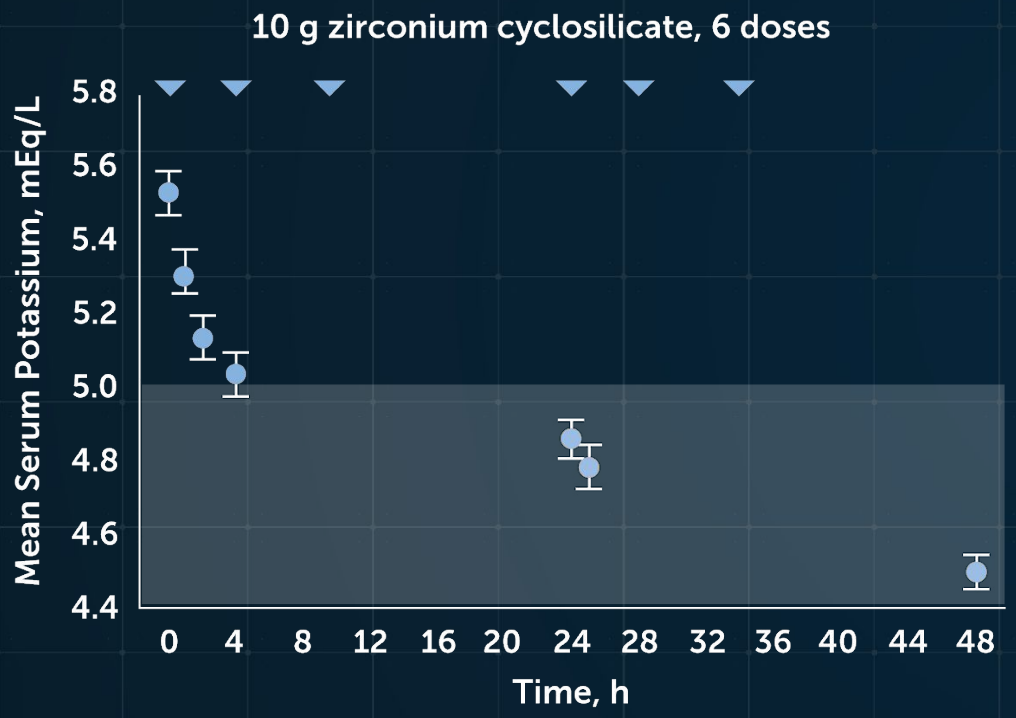
Bakris GL, et al. *JAMA*. 2015;314(2):151–161.

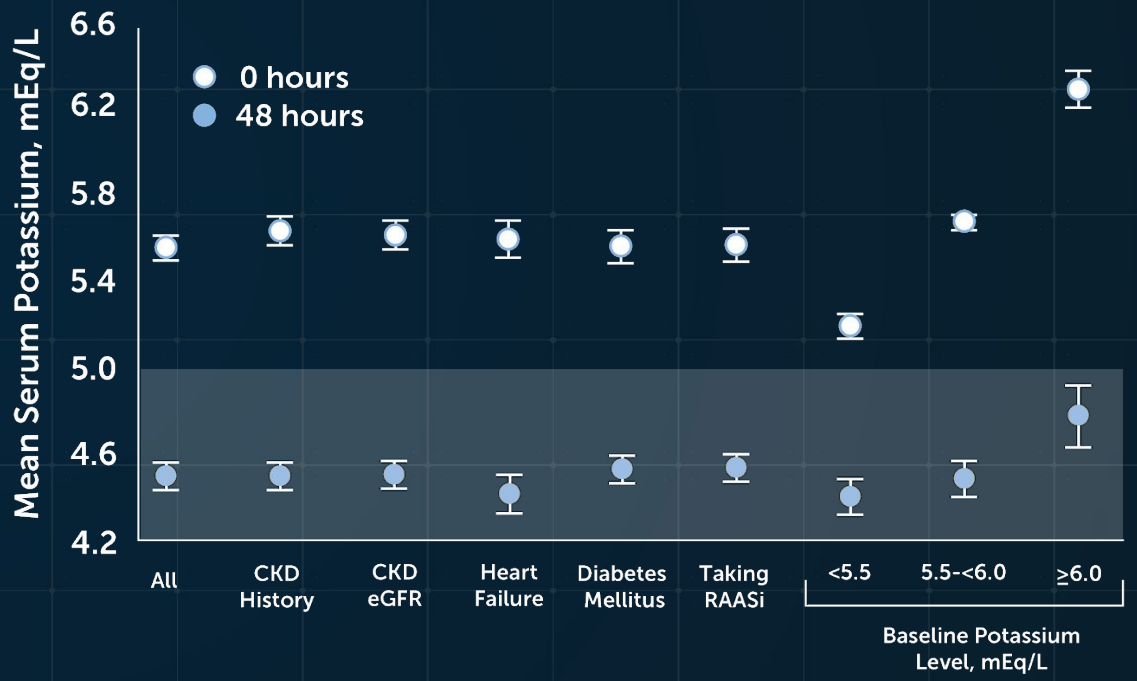
Sodium Zirconium Cyclosilicate (SZC)

- Inorganic crystal
- Exchanges K^+ for Na^+ or H^+
- May bind K^+ in higher portions of the GI tract

HARMONIZE: SZC Normalizes Serum K^+

Patients with hyperkalemia (K^+ ≥5.1 mmol/L), N = 258



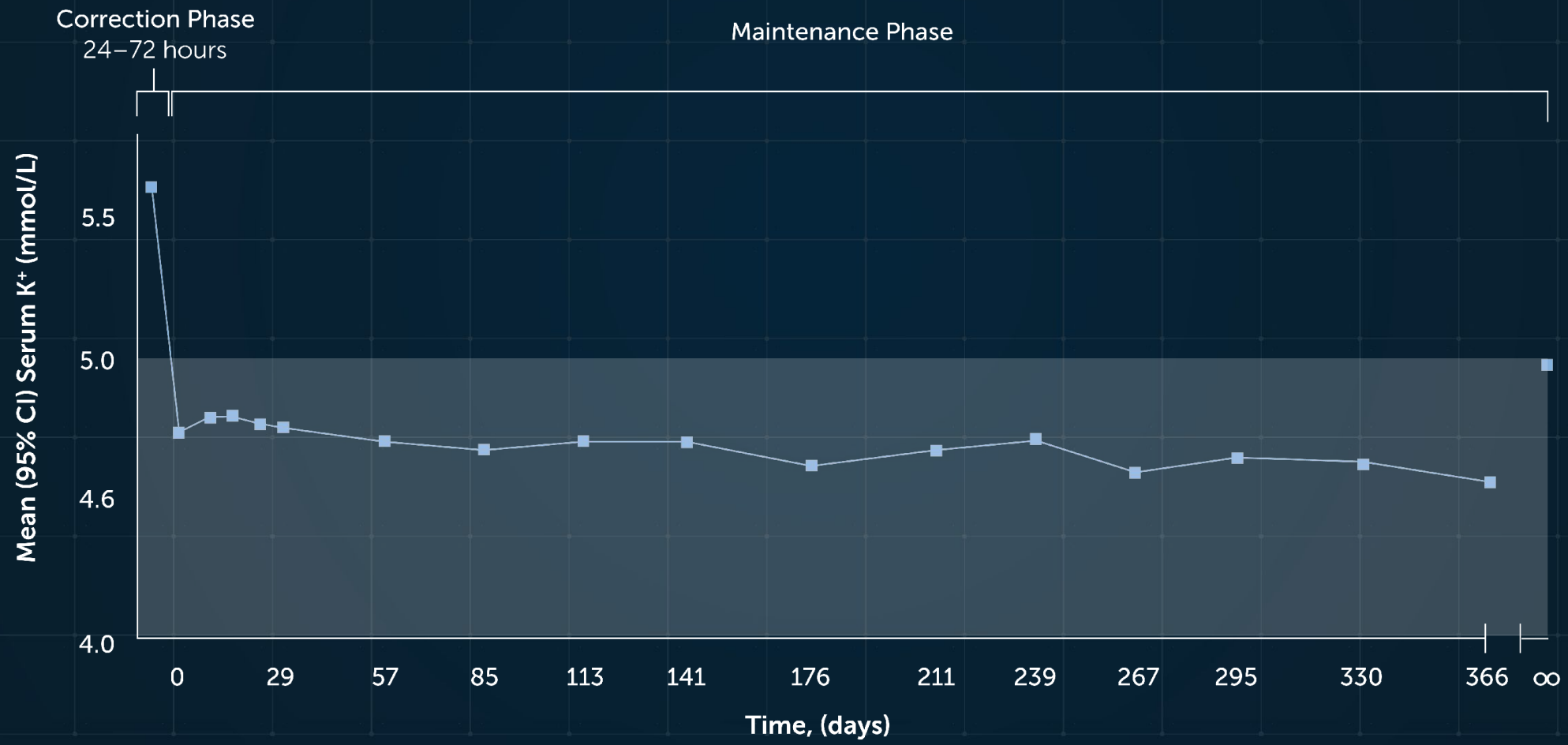


No. of patients									
0 hours	258	169	179	94	170	180	119	100	39
48 hours	251	163	172	92	166	173	115	99	37

SZC = sodium zirconium cyclosilicate; Kosiborod M, et al. *JAMA*. 2014;312(21):2223-2233.

ZS-005: SZC Maintains Normokalemia

Patients with hyperkalemia ($K^+ \geq 5.1$ mmol/L), N = 751



SZC = sodium zirconium cyclosilicate; Spinowitz BS, et al. *Clin J Am Soc Nephrol*. 2019;14(6):798-809.

ZS-005: SZC Adverse Events

- Nausea 8%
- Constipation 6%
- Vomiting 5%
- Hypokalemia 2%
- Peripheral edema 10%

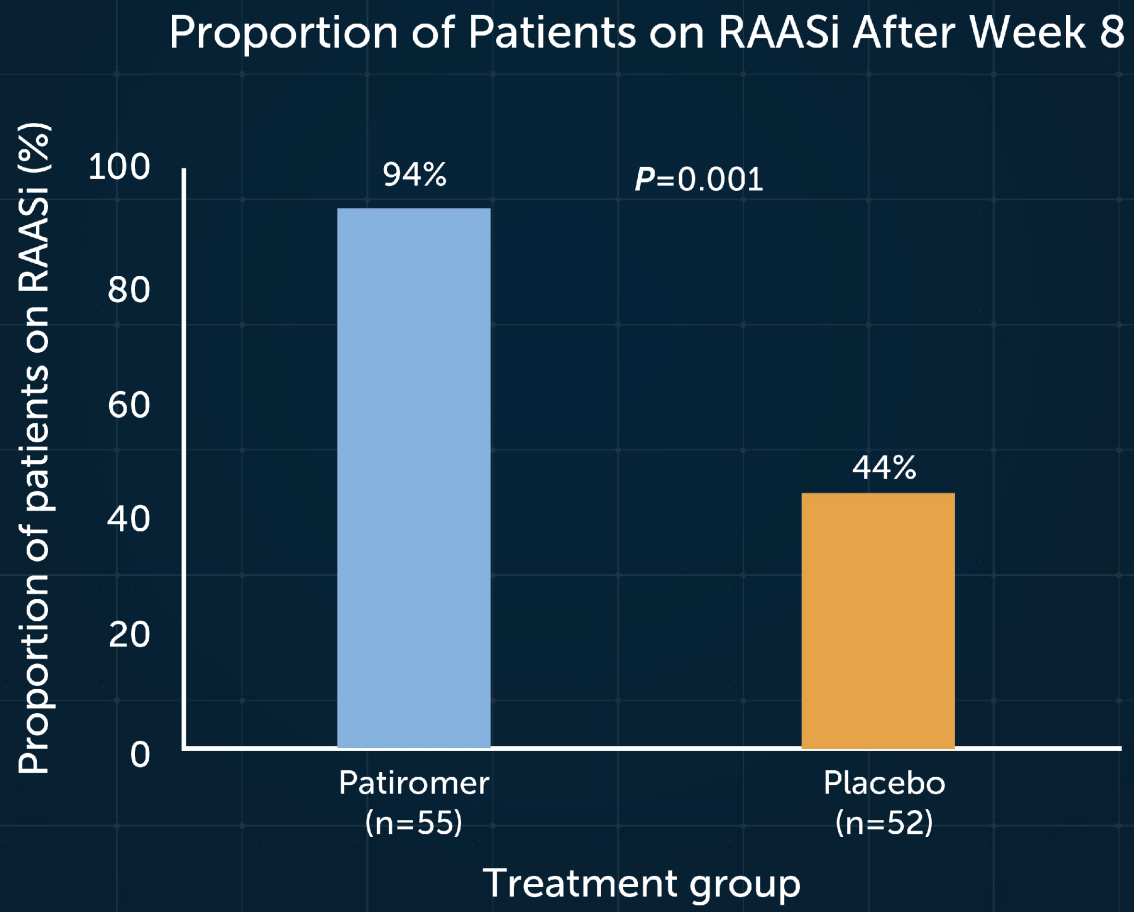
SZC = sodium zirconium cyclosilicate; Spinowitz BS, et al. *Clin J Am Soc Nephrol*. 2019;14(6):798-809.

Upcoming Clinical Trials

- DIAMOND
  - To determine if patiromer treatment allows for continued use of RAASi therapy and decrease CV risk in patients with HFrEF and hyperkalemia
- PRIORITIZE HF
  - To evaluate whether SZC can help optimize RAASi therapy in patients with HFrEF and hyperkalemia

clinicaltrials.gov/ct2/show/NCT03888066; clinicaltrials.gov/ct2/show/NCT03532009

OPAL-HK: Patiromer Enables RAASi Continuation



RAASi = renin-angiotensin-aldosterone system inhibitor; Weir MR, et al. *N Engl J Med.* 2015;372(3):211–221.

When starting a potassium binder:

- Check K^+ level
- If significantly elevated, monitor frequently
- For mild to moderate hyperkalemia
  - Monitor K^+ 1 week after starting the binder
  - Continue monitoring at 2 weeks, then 4 weeks if stable
  - If up titrating RAASi therapy, then monitor more frequently

Stockholm Creatinine Measurements (SCREAM) Project

- 23,927 new users of ACE-I or ARB
- Only 34% had K^+ checked within 1 month of initiation

Bandak G, et al. *J Am Heart Assoc*. 2017;6(7):e005428.

Clinical Pearls

- Appropriate K^+ is critical
- Novel potassium binders are titratable