A Phase 3b, Randomized, Double-Blind, Placebo-Controlled Study of Sodium Zirconium Cyclosilicate for Reducing the Incidence of Predialysis Hyperkalemia

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Supplementary Materials

Table of Contents

Methods

Study Treatments

Study treatments were provided as a powder for oral suspension in a sachet. A single dose contained 1 to 3 sachets that was suspended in 45 mL of water by the patient and administered on non-dialysis days. Doses were provided as follows: 5 g = one sachet, 10 g = two sachets, and 15 g = three sachets. The PBO was silicified microcrystalline cellulose, NF, a commercially available product which is received and used in the pure form.

Randomization and Blinding

Randomization was performed using randomization codes and an interactive voice/interactive web response system. Randomization codes were generated in blocks of 4 (2 + 2 for each treatment arm) to ensure balance (1:1) between the two treatment arms. Randomization was stratified by country. Study site staff and patients were blinded to treatment assignment. To ensure blinding, sachets were enclosed in a carton with a tamper evident seal intended to be broken exclusively by patients immediately before taking the study drug.

Dose Titration

The starting dose of SZC and PBO was 5 g once daily and was adjusted to a maximum of 15 g on non-dialysis days to maintain a predialysis sK^+ concentration of 4.0–5.0 mmol/L. All dose adjustments were based on predialysis sK^+ measured by i-STAT. During the first 4 weeks of the treatment period, the SZC and PBO doses were adjusted if the predialysis sK^+ after the long interdialytic interval was

>5.0 mmol/L (one weekly dose adjustment). For patients taking 5 g on non-dialysis days, the dose was increased to 10 g on non-dialysis days. For patients taking 10 g, the dose was increased to 15 g on non-dialysis days.

For predialysis sK^+ concentrations <4 mmol/L, subsequent adjustments in dK^+ concentration were made in accordance with locally accepted clinical practice patterns and guided by the investigator's clinical judgment. For centers that adopted the clinical practice of modifying the prescribed dK^+ concentration when the predialysis sK^+ concentration decreased, if predialysis sK^+ was <4 mmol/L the dK^+ concentration was increased by 0.5 or 1.0 mmol/L according to standard of care, *e.g.,* increase dK^+ from 1K to 1.5 or 2K, from 2K to 2.5 or 3K, or from 3K to 3.5 or 4K. If dK^+ concentration could not be increased further (*e.g.,* patient was already using 4K dialysate bath), the dose could be decreased by 5 g or held if the patient was already taking the minimum dose (5 g). For sites in which local clinical practice did not include increasing the dK^+ concentration when predialysis sK^+ fell, the dose of SZC or PBO could be decreased by 5 g or held if the patient was already taking the minimum dose (5 g).

If during the treatment phase (initial 4 weeks) the dose of SZC or PBO was reduced or held and the predialysis sK^+ after the next long interdialytic interval was >5.0 mmol/L, every effort was made to increase the dose by 5 g or restart 5 g if it was held.

Inclusion Criteria

- Provision of informed consent prior to any study specific procedures.
- Females or males aged ≥18 years at screening (Visit 1). For patients aged

<20 years and enrolled in Japan, a written informed consent was obtained from the patient and his or her legally acceptable representative.

- Receiving HD (or hemodiafiltration) three times weekly for treatment of ESRD for at least 3 months before randomization.
- Patients had HD access consisting of an arteriovenous fistula, arteriovenous graft, or tunnelled (permanent) catheter, which was expected to remain in place for the entire duration of the study.
- Predialysis sK^+ >5.4 mmol/L after the long interdialytic interval and >5.0 mmol/L after one short interdialytic interval during screening (as assessed by the central laboratory).
- Prescribed dK^+ ≤3 mmol/L during screening.
- Sustained blood flow ≥200 mL/min and single-pool Kt/V ≥1.2 (or urea reduction ratio ≥63) on stable HD/hemodiafiltration prescription during screening with prescription (time, dialyser, sustained blood flow, dialysate flow rate, and bicarbonate concentration) expected to remain unchanged during study.
- Heparin dose (if used) was stable during screening and expected to be stable during the study.
- Patients were receiving dietary counselling appropriate for patients with ESRD treated with HD/hemodiafiltration as per local guidelines, which included dietary potassium restriction.

Exclusion Criteria

- Involvement in the planning and/or conduct of the study.
- Hemoglobin <9 g/dL at screening (as assessed on Visit 1).
- Lack of compliance with HD prescription (both number and duration of treatments) during the 2-week period preceding screening (100% compliance required).
- Patients treated with sodium polystyrene sulfonate, calcium polystyrene sulfonate, or patiromer within 7 days before screening or anticipated in requiring any of these agents during the study.
- Myocardial infarction, acute coronary syndrome, stroke, seizure, or a thrombotic/thromboembolic event (*e.g.,* deep vein thrombosis or pulmonary embolism, but excluding vascular access thrombosis) within 12 weeks prior to randomization.
- Laboratory diagnosis of hypokalemia (sK^+ <3.5 mmol/L), hypocalcemia (calcium <8.2 mg/dL; for Japan, hypocalcemia defined as albumin-corrected calcium <8.0 mg/dL), hypomagnesemia (magnesium <1.7 mg/dL), or severe acidosis (serum bicarbonate ≤16 mEq/L) in the 4 weeks preceding randomization.
- Pseudohyperkalemia secondary to hemolyzed blood specimen (this situation was not considered screening failure; sampling or full screening could be postponed to a later time as applicable).
- Severe leucocytosis (>20 × 10^9/L) or thrombocytosis (≥450 × 10^9/L) during screening.
- Polycythemia (hemoglobin >14 g/dL) during screening.

- Diagnosis of rhabdomyolysis during the 4 weeks preceding randomization.
- Patients treated with lactulose, rifaximin, or other non-absorbed antibiotics for hyperammonemia within 7 days prior to the first dose of study drug.
- Patients unable to take oral SZC drug mix.
- Scheduled date for living donor kidney transplant.
- Patients with a life expectancy of less than 6 months.
- Female patients who were pregnant or breastfeeding.
- Females of childbearing potential, unless using contraception or sexual abstinence.
- Known hypersensitivity or previous anaphylaxis to SZC or to components thereof.
- Participation in another clinical study with an investigational product during 1 month before screening.
- Any medical condition (including active clinically significant infection) that in the opinion of the investigator or sponsor may have posed a safety risk to a patient in this study, which may have confounded safety or efficacy assessment and jeopardized the quality of the data, or interfered with study participation.
- Presence of cardiac arrhythmias or conduction defects that required immediate treatment.
- History of alcohol or drug abuse within 2 years prior to randomization.
- Previous randomization in the present study.

Study Assessments

During screening, consenting patients were assessed to ensure eligibility criteria were met. Predialysis central laboratory sK^+ samples were collected at Visit 1 (Day –7, long interdialytic interval), Visit 2 (Day –5, short interdialytic interval), and Visit 3 (Day –3, short interdialytic interval). Demographics and medical/surgical history were collected at Visit 1 (Day –7). dK^+ prescription was recorded at Visits 1 to 3. Dialysis prescription (blood flow and time on dialysis) and adequacy (single-pool Kt/V and/or urea removal rate) were assessed at Visit 1 (Day –7); the latter was recorded as the most recent value but could be no older than 5 weeks.

A complete physical examination was performed on Days –7 and 1, and at follow-up, and included the following: general appearance, skin, height (Day –7 only) and weight, head and neck, lymph nodes, thyroid, musculoskeletal (including spine and extremities), respiratory, cardiovascular including assessment of signs of heart failure, abdomen, and neurological systems. A targeted physical examination was performed on Days 8, 15, 22, and 50, and included the following: weight (weighed on the same scale in the same state of dress), skin, extremities, respiratory, cardiovascular including assessment of signs of heart failure, and abdomen.

To obtain all required measurements of IDWG, the investigators made sure that a post-dialysis weight was available for the immediate dialysis session (as per usual schedule) prior to the visit.

Safety laboratory assessments were performed at Days –7, 1 (randomization), 15, 22, 50, and 57, and follow-up. Assessments included hemoglobin, leukocytes, platelets, creatinine, bilirubin, alkaline phosphatise, aspartate transaminase, alanine transaminase, gamma-glutamyl transferase, albumin, potassium, calcium, sodium,

chloride, creatine kinase, bicarbonate, phosphorus, glucose, blood urea nitrogen, magnesium, lactate dehydrogenase, total protein, and pregnancy test (serum human chorionic gonadotropin).

Vital signs were assessed at Day –7, weekly, and at follow-up. Heart rate and blood pressure were measured in triplicate after the patient had been comfortably at rest in either supine or seated position for at least 5 minutes.

A 12-lead ECG was performed predialysis on Days –7, 8, and 29, as well as follow-up, and was assessed by investigators according to local practice. ECGs were classified as normal, borderline, abnormal–not clinically significant, and abnormal–clinically significant.

Study Endpoints

All AEs were classified using the Medical Dictionary for Regulatory Activities version 21.1. AEs were recorded from time of randomization through to follow-up, and SAEs were recorded from the time of informed consent. Variables collected for AEs included:

- whether the AE was serious or non-serious
- maximum intensity
- outcome (death or no death)
- whether the AE led to treatment discontinuation or not
- investigator causality rating.

IDWG was calculated as the difference between current predialysis weight minus previous post-dialysis weight (measured at immediate dialysis session prior to the visit). Baseline IDWG was defined as the latest IDWG calculated over the long interdialytic interval during screening.

Results

Baseline Patient Characteristics

Medical history was generally balanced between treatment groups, with the exception of cardiac disorders (46.4% versus 61.6% in SZC versus PBO, respectively); congenital, familial, and genetic disorders (6.2% versus 14.1%); eye disorders (24.7% versus 33.3%); general disorders and administration site conditions (*e.g.,* administration site erythema, pain and reactions) (12.4% versus 20.2%); investigations (3.1% versus 9.1%); nervous system disorders (50.5% versus 40.4%); and respiratory, thoracic, and medical disorders (22.7% versus 31.3%).

Mean sK^+ Levels

Mean predialysis sK^+ in the SZC group decreased to 5.0 (0.5) mmol/L by the end of the dose-titration period, remained stable throughout the evaluation period (range, 4.9–5.1 mmol/L), and increased at Visit 16 (end of study). With PBO, predialysis sK^+ was stable throughout the dose-titration period (range, 5.5–5.8 mmol/L) and evaluation period (range, 5.5–5.9 mmol/L), and remained high at end of study. Mean post-dialysis sK^+ in the SZC and PBO groups showed similar changes over time to those of predialysis sK^+ levels in the corresponding treatment groups, but the magnitude of change was lower.

Treatment Exposure

Total mean exposure to treatment during the overall treatment period was 52.8 days and was balanced between treatment groups (SZC, 52.0 days; PBO, 53.5 days).

There was no difference in duration of exposure between the dose-adjustment period (26.2 days) and the evaluation period (26.8 days).

Supplemental Table 1. Failed inclusion and exclusion criteria for non-randomized patients (all patients)

Criteria	*n*
Inclusion criteria	
Predialysis sK^+ >5.4 mmol/L after LIDI and >5.0 mmol/L after one SIDI during screening (as assessed by central laboratory)	154
Sustained blood flow ≥200 mL/min and spKt/V ≥1.2 (or URR ≥63) on stable HD/hemodiafiltration prescription during screening with prescription expected to remain unchanged during study	6
Patients must have HD access consisting of an arteriovenous fistula, AV graft, or tunnelled (permanent) catheter that is expected to remain in place for the entire duration of the study	2
Provision of informed consent prior to any study specific procedures	2
Heparin dose (if used) must be stable during screening and expected to be stable during the study	1
Receiving HD (or hemodiafiltration) three times weekly for treatment of ESRD for ≥3 months before randomization	1
Patients must be receiving dietary counselling appropriate for ESRD patients treated with HD/hemodiafiltration as per local guidelines, which includes dietary potassium restriction	1
Exclusion criteria	
Laboratory diagnosis of hypokalemia, hypocalcemia, hypomagnesemia, or severe acidosis in the 4 weeks preceding randomization	63
Pseudohyperkalemia secondary to hemolyzed blood specimen (this situation is not considered screening failure, sampling or full screening can be postponed to a later time as applicable)	42
Hemoglobin <9 g/dL on screening (as assessed on Visit 1)	25
Myocardial infarction, acute coronary syndrome, stroke, seizure, or a thrombotic/thromboembolic event within 12 weeks prior to randomization	6
Polycythemia (hemoglobin >14 g/dL) during screening	5
Severe leukocytosis (>20 × 10^9/L) or thrombocytosis (≥450 × 10^9/L) during screening	4
Lack of compliance with HD prescription (both number and duration of treatments) during the 2-week period preceding screening (100% compliance required)	3
Presence of cardiac arrhythmias or conduction defects that require immediate treatment	2
Any medical condition that may pose a safety risk to a patient in this study, which may confound safety or efficacy assessment and jeopardize the quality of the data	1
History of alcohol or drug abuse within 2 years prior to randomization	1

Criteria	***n***
Involvement in the planning and/or conduct of the study (applies to both AstraZeneca, including SZC Pharma staff, and/or staff at the study site)	1
Patients treated with sodium polystyrene sulfonate or calcium polystyrene sulfonate within 7 days before screening or anticipated in requiring any of these agents during the study	1
Patients unable to take oral SZC drug	1

AV, arteriovenous; ESRD, end-stage renal disease; HD, hemodialysis; LIDI, long interdialytic interval; SIDI, short interdialytic interval; sK^+, serum potassium; spKt/V, single-pool Kt/V; SZC, sodium zirconium cyclosilicate; URR, urea reduction ratio.

Supplemental Table 2. sK^+ responder groupings (full analysis set)

	Patients, *n* (%)	
	SZC (*n*=97)	**PBO (*n*=99)**
Responders[a]	40 (41.2)	1 (1.0)
Non-responders[b]	57 (58.8)	98 (99.0)
>1 missing sK^+ measurement	8 (8.2)	10 (10.1)
Received rescue therapy	1 (1.0)	2 (2.0)
<3 predialysis sK^+ measurements between 4.0 and 5.0 mmol/L	57 (58.8)	98 (99.0)

PBO, placebo; sK^+, serum potassium; SZC, sodium zirconium cyclosilicate.

[a]Responders were defined as patients who, during the evaluation period, maintained a predialysis sK^+ between 4.0 and 5.0 mmol/L during ≥3 out of 4 dialysis treatments following the long interdialytic interval and who did not receive rescue therapy.

[b]An individual patient could be classed as a non-responder for more >1 reason but was only counted once as a non-responder.

Supplemental Table 3. Patients with predialysis sK^+ measurements between 4.0 and 5.0 mmol/L or 3.5 and 5.5 mmol/L during the evaluation period (full analysis set)

	Patients, *n* (%)	
	SZC (*n*=97)	**PBO (*n*=99)**
Number of sK^+ measurements between 4.0 and 5.0 mmol/L		
At least 1	76 (78.4)	26 (26.3)
At least 2	56 (57.7)	12 (12.1)
At least 3	40 (41.2)	1 (1.0)
At least 4	23 (23.7)	0 (0.0)
Number of sK^+ measurements between 3.5 and 5.5 mmol/L		
At least 1	92 (94.8)	67 (67.7)
At least 2	84 (86.6)	35 (35.4)
At least 3	68 (70.1)	21 (21.2)
At least 4	50 (51.5)	5 (5.1)

Includes predialysis sK^+ values obtained at the long interdialytic interval visits in the evaluation period.

PBO, placebo; sK^+, serum potassium; SZC, sodium zirconium cyclosilicate.

Supplemental Table 4. Mean pre- and post-dialysis sK^+ at each visit for patients treated with SZC (*n*=97) and PBO (*n*=99) (full analysis set)

		SZC (*n*=97)		PBO (*n*=99)	
Study visit	**Summary statistic**	**Predialysis**	**Post-dialysis[a]**	**Predialysis**	**Post-dialysis[a]**
1[b] (Day –7)	*n*	95	NA	99	NA
	Mean	6.0		6.0	
	SD	0.4		0.4	
2 (Day –5)	*n*	86	NA	92	NA
	Mean	5.7		5.8	
	SD	0.5		0.5	
3 (Day –3)	*n*	81	NA	88	NA
	Mean	5.6		5.6	
	SD	0.5		0.5	
4[b] (Day 1) (randomization)	*n*	81	93	86	95
	Mean	5.8	3.8	5.9	3.9
	SD	0.6	0.6	0.6	0.6
7[b] (Day 8)	*n*	89	90	86	93

		SZC (*n*=97)		PBO (*n*=99)	
Study visit	**Summary statistic**	**Predialysis**	**Post-dialysis[a]**	**Predialysis**	**Post-dialysis[a]**
	Mean	5.4	3.7	5.8	3.9
	SD	0.6	0.5	0.6	0.7
9[b] (Day 15)	*n*	90	91	87	93
	Mean	5.2	3.7	5.7	3.8
	SD	0.5	0.6	0.5	0.5
10[b] (Day 22)	*n*	93	92	89	93
	Mean	5.1	3.6	5.8	3.8
	SD	0.6	0.6	0.6	0.5
11[b] (Day 29)	*n*	92	95	88	95
	Mean	5.0	3.6	5.7	3.8
	SD	0.5	0.6	0.6	0.6
12[b] (Day 36)	*n*	88	88	86	93
	Mean	5.0	3.6	5.7	3.8
	SD	0.5	0.6	0.6	0.6
13[b] (Day 43)	*n*	90	91	88	95
	Mean	5.0	3.6	5.7	3.8

		SZC (*n*=97)		PBO (*n*=99)	
Study visit	**Summary statistic**	**Predialysis**	**Post-dialysis[a]**	**Predialysis**	**Post-dialysis[a]**
	SD	0.6	0.6	0.7	0.5
14[b] (Day 50)	*n*	90	88	90	92
	Mean	5.0	3.5	5.9	3.9
	SD	0.6	0.4	0.7	0.5
15[b] (Day 57) (EOT)	*n*	82	84	90	93
	Mean	5.1	3.6	5.7	3.9
	SD	0.6	0.6	0.7	0.6
16 (Day 71) (EOS)	*n*	87	92	91	97
	Mean	5.6	3.8	5.7	3.8
	SD	0.7	0.6	0.8	0.5

Visits 7 to 11 were part of the dose-adjustment treatment period. Visits 12 to 15 were part of the evaluation treatment period. EOS, end of study; EOT, end of treatment; NA, not available; PBO, placebo; SD, standard deviation; sK^+, serum potassium; SZC, sodium zirconium cyclosilicate.

[a]Post-dialysis assessments were not collected at all visits, represented by NA; [b]long interdialytic interval visit.

Supplemental Table 5. Proportions of patients with maximum sK^+ concentrations ≥6.0 mmol/L following the long interdialytic intervals during the evaluation period (full analysis set)

	Maximum sK^+ concentration following the long interdialytic intervals during the evaluation period (mmol/L)		
Treatment	**6–6.5**	**6.5–7**	**≥7**
PBO (*n*=99)	30 (73.2)	13 (92.9)	13 (86.7)
SZC (*n*=97)	11 (26.8)	1 (7.1)	2 (13.3)
Total	41	14	15

Data shown are number (%) of patients. Percentages are based on the total numbers of patients in the sK^+ concentration strata. PBO, placebo; sK^+, serum potassium; SZC, sodium zirconium cyclosilicate.

Supplemental Table 6. Mean intradialytic potassium shift by study visit (full analysis set)

Study visit	Summary statistic	SZC (*n*=97)	PBO (*n*=99)
4 (Day 1) (randomization)	*n*	80	85
	Mean	2.0	2.1
	SD	0.7	0.7
7 (Day 8)	*n*	87	84
	Mean	1.7	1.9
	SD	0.7	0.9
9 (Day 15)	*n*	88	86
	Mean	1.5	1.9
	SD	0.7	0.6
10 (Day 22)	*n*	91	86
	Mean	1.5	2.0
	SD	0.7	0.7
11 (Day 29)	*n*	92	88
	Mean	1.4	1.9
	SD	0.8	0.7
12 (Day 36)	*n*	86	86
	Mean	1.4	1.9
	SD	0.7	0.8
13 (Day 43)	*n*	90	88
	Mean	1.5	1.9
	SD	0.6	0.8
14 (Day 50)	*n*	88	88
	Mean	1.4	2.0
	SD	0.7	0.7
15 (Day 57) (EOT)	*n*	81	88

Study visit	Summary statistic	SZC (*n*=97)	PBO (*n*=99)
	Mean	1.5	1.9
	SD	0.6	0.9
16 (Day 71) (EOS)	*n*	84	90
	Mean	1.9	1.9
	SD	0.7	0.8

Intradialytic potassium shift was defined as the difference between predialysis sK^+ and post-dialysis sK^+. Visits 7 to 11 were part of the dose-adjustment treatment period. Visits 12 to 15 were part of the evaluation treatment period. EOS, end of study; EOT, end of treatment; PBO, placebo; SD, standard deviation; sK^+, serum potassium; SZC, sodium zirconium cyclosilicate.

Supplemental Table 7. Mean dialysis potassium gradient by study visit (full analysis set)

Study visit	Summary statistic	SZC (*n*=97)	PBO (*n*=99)
4[a] (Day 1) (randomization)	*n*	81	86
	Mean	3.6	3.7
	SD	0.7	0.6
5 (Day 3)	*n*	91	94
	Mean	3.3	3.3
	SD	0.7	0.7
6 (Day 5)	*n*	90	89
	Mean	3.1	3.3
	SD	0.6	0.6
7[a] (Day 8)	*n*	89	86
	Mean	3.1	3.5
	SD	0.8	0.7
8 (Day 12)	*n*	92	94
	Mean	2.8	3.3
	SD	0.7	0.7
9[a] (Day 15)	*n*	90	87
	Mean	2.9	3.4
	SD	0.7	0.6
10[a] (Day 22)	*n*	93	89
	Mean	2.8	3.5
	SD	0.7	0.8
11[a] (Day 29)	*n*	92	88
	Mean	2.7	3.5
	SD	0.8	0.7
12[a] (Day 36)	*n*	88	86
	Mean	2.7	3.5
	SD	0.7	0.7
13[a] (Day 43)	*n*	90	88
	Mean	2.7	3.5
	SD	0.8	0.6
14[a] (Day 50)	*n*	90	90

Study visit	Summary statistic	SZC (*n*=97)	PBO (*n*=99)
	Mean	2.7	3.6
	SD	0.8	0.7
15[a] (Day 57) (EOT)	*n*	82	89
	Mean	2.8	3.5
	SD	0.8	0.7
16 (Day 71) (EOS)	*n*	86	91
	Mean	3.4	3.5
	SD	0.8	0.9

Dialysis potassium gradient was defined as the difference between predialysis sK^+ and the dK^+ concentration.

Visits 7 to 11 were part of the dose-titration period. Visits 12 to 15 were part of the evaluation period.

dK^+, dialysate potassium; EOS, end of study; EOT, end of treatment; PBO, placebo; SD, standard deviation; sK^+, serum potassium; SZC, sodium zirconium cyclosilicate.

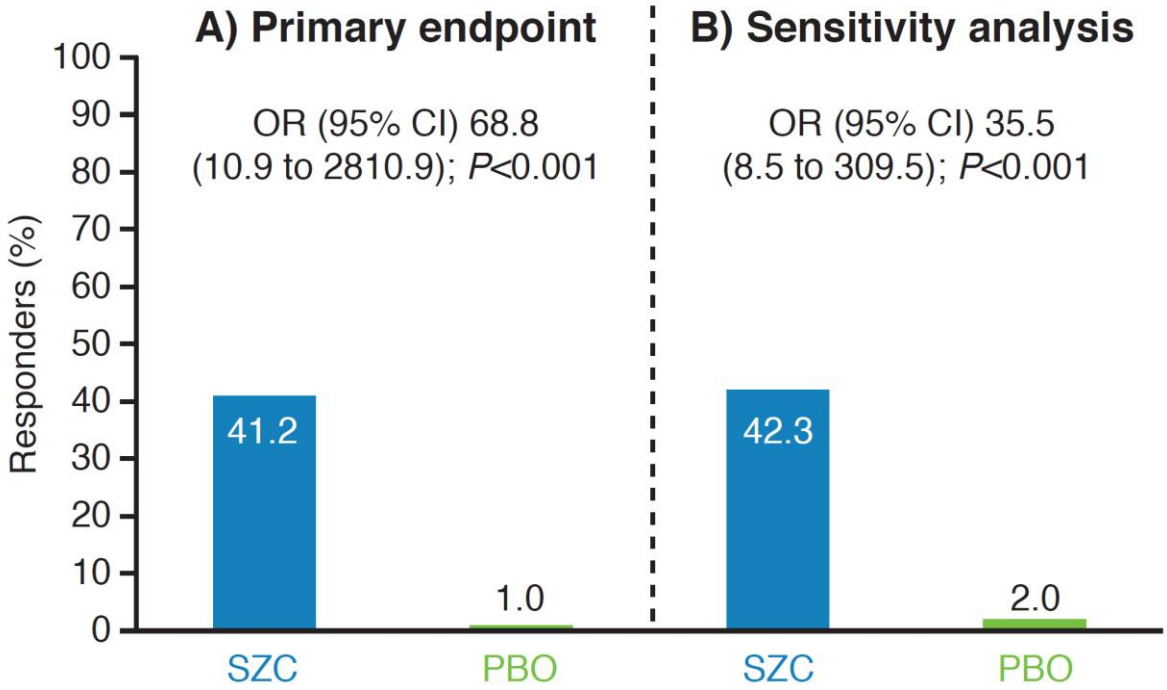
[a]Long interdialytic interval visit.

Supplemental Table 8. IDWG over time (safety analysis set)

	SZC (*n*=96)			PBO (*n*=99)		
Timepoint	***n***	**Mean (SD) value**	**Mean (SD) change from baseline**	***n***	**Mean (SD) value**	**Mean (SD) change from baseline**
Baseline	96	3.0 (1.3)	–	99	2.9 (1.6)	–
Visit 11 (Day 29)	95	2.7 (3.7)	–0.3 (3.6)	97	2.8 (1.5)	–0.1 (1.5)
Visit 15 (Day 57; EOT)	83	3.2 (1.3)	0.2 (1.3)	88	2.7 (1.6)	–0.1 (1.6)

IDWG was calculated as predialysis weight minus post-dialysis weight (after the previous immediate dialysis session) in kg. Baseline IDWG was defined as the latest IDWG calculated over the long interdialytic interval during screening that occurred immediately prior to Visit 4 (Day 1). EOT, end of treatment; IDWG, interdialytic weight gain; PBO, placebo; SD, standard deviation; SZC, sodium zirconium cyclosilicate.

Supplemental Figure 1. Proportion of patients that achieved target sK^+ during ≥3 out of 4 measurements and did not require rescue therapy in the SZC and PBO groups in the (A) full analysis set and (B) sensitivity analysis



Responders were defined as patients who, during the evaluation period, maintained a predialysis sK^+ between 4.0 and 5.0 mmol/L during ≥3 out of 4 dialysis treatments following the LIDI and who did not receive rescue therapy; *P* value obtained using a two-sided Fisher's exact test. PBO was the reference treatment. The *P* value, and not CI for OR, was used for the decision of rejection or acceptance of the null hypothesis. The sensitivity analysis was conducted to determine the impact of being classified as a non-responder due to missing sK^+ data. Missing central laboratory sK^+ measurements were replaced using available i-STAT data adjusted for the mean paired difference between the values in patients with both values available at the relevant time point.

CI, confidence interval; LIDI, long interdialytic interval; OR, odds ratio; PBO, placebo; sK^+, serum potassium; SZC, sodium zirconium cyclosilicate.