SUPPLEMENTARY MATERIALS

Real-World Modifications of Renin-Angiotensin-Aldosterone System Inhibitors in Patients with Hyperkalemia Initiating Sodium Zirconium Cyclosilicate Therapy: The OPTIMIZE I Study

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Sample	N	Optimi Maintained same RAASi dose	zed dose Increased RAASi dose	Non-optimized dose Discontinued RAASi Decreased therapy RAASi dose		
· · · · · · · · · · · · · · · · · · ·				therapy		
Stage 3 CKD ¹	171	118 (69.0%)	19 (11.1%)	23 (13.5%)	11 (6.4%)	
Stage 4 CKD ¹	174	121 (69.5%)	12 (6.9%)	31 (17.8%)	10 (5.7%)	
Stage 5 CKD ¹	33	24 (72.7%)	2 (6.1%)	4 (12.1%)	3 (9.1%)	
Stage 5 CKD or ESKD ²	150	106 (70.7%)	6 (4.0%)	30 (20.0%)	8 (5.3%)	
ESKD ³	117	82 (70.1%)	4 (3.4%)	26 (22.2%)	5 (4.3%)	
HF	149	95 (63.8%)	19 (12.8%)	29 (19.5%)	6 (4.0%)	
Hypertension	538	376 (69.9%)	40 (7.4%)	92 (17.1%)	30 (5.6%)	

Supplementary Table 1. RAASi Modifications After SZC Initiation Among Additional Subgroups

Abbreviations: CKD, chronic kidney disease; ESKD, end-stage kidney disease; HF, heart failure; RAASi, reninangiotensin-aldosterone system inhibitors; SZC, sodium zirconium cyclosilicate

¹CKD Stage 3-5 was s assessed using ICD-10 diagnosis codes.

²Stage 5 CKD or ESKD includes all patients with either Stage 5 CKD or ESKD.

³ ESKD was assessed using ICD-10 diagnosis codes for ESKD or an ICD-10 diagnosis code for CKD stage 5 + a code for dialysis.

	All patients (N=472)	Optimized RAASi ² (N=370)	Did not optimize RAASi ³ (N=102)	p-value
Demographics	(1, 1, 2)	(11 010)	(11 102)	p vulue
Age on index date (years), mean \pm SD	62.36 ± 12.60	62.03 ± 12.60	63.54 ± 12.58	0.39
Female gender, n (%)	162 (34.3%)	136 (36.8%)	26 (25.5%)	< 0.05*
Claims payer, n (%)				0.14
Commercial or unknown	218 (46.2%)	175 (47.3%)	43 (42.2%)	
Medicaid	102 (21.6%)	84 (22.7%)	18 (17.6%)	
Medicare Advantage	152 (32.2%)	111 (30.0%)	41 (40.2%)	
Region, n (%)		()		0.78
Midwest	62 (13.1%)	50 (13.5%)	12 (11.8%)	
Northeast	117 (24.8%)	89 (24.1%)	28 (27.5%)	
South	169 (35.8%)	135 (36.5%)	34 (33.3%)	
West	119 (25.2%)	91 (24.6%)	28 (27.5%)	
Other	5 (1.1%)	5 (1.4%)	0 (0.0%)	
НК				
HK diagnosis, n (%)	291 (61.7%)	221 (59.7%)	70 (68.6%)	0.13
Comorbidities, n (%)		× ,		
CKD stages 3-5	398 (84.3%)	314 (84.9%)	84 (82.4%)	0.64
Congestive heart failure	101 (21.4%)	80 (21.6%)	21 (20.6%)	0.93
Coronary artery disease	122 (25.8%)	92 (24.9%)	30 (29.4%)	0.42
Diabetes	336 (71.2%)	263 (71.1%)	73 (71.6%)	1.00
Hypertension	427 (90.5%)	336 (90.8%)	91 (89.2%)	0.77
Prior Treatment, n (%)				
HK treatments				
Patiromer	88 (18.6%)	70 (18.9%)	18 (17.6%)	0.88
Sodium polystyrene sulfonate	77 (16.3%)	55 (14.9%)	22 (21.6%)	0.14
Loop diuretics	201 (42.6%)	153 (41.4%)	48 (47.1%)	0.36
Thiazides and thiazide-like diuretics	88 (18.6%)	69 (18.6%)	19 (18.6%)	1.00
Other treatments				
Beta blockers	281 (59.5%)	220 (59.5%)	61 (59.8%)	1.00
NSAIDs	40 (8.5%)	33 (8.9%)	7 (6.9%)	0.65
All-Cause HRU				
Any inpatient stays, n (%)	103 (21.8%)	76 (20.5%)	27 (26.5%)	0.25
Number of inpatient stays, mean \pm SD	0.37 ± 0.88	0.33 ± 0.78	0.51 ± 1.16	0.18
Any ED visits, n (%)	128 (27.1%)	91 (24.6%)	37 (36.3%)	< 0.05*
Number of ED visits, mean \pm SD	0.41 ± 0.87	0.36 ± 0.84	0.59 ± 0.97	< 0.05*
Any outpatient visits, n (%)	434 (91.9%)	344 (93.0%)	90 (88.2%)	0.18
Number of outpatient visits, mean \pm SD	13.38 ± 14.75	12.98 ± 13.59	14.85 ± 18.35	0.53

Supplementary Table 2. Baseline Characteristics of Patients Without ESKD Initiating SZC¹

Abbreviations: CKD, chronic kidney disease; ED, emergency department; ESKD, end-stage kidney disease; HK, hyperkalemia; HRU, healthcare resource utilization; NSAID, non-steroidal anti-inflammatory drug; SD, standard deviation; SZC, sodium zirconium cyclosilicate

¹Baseline was the 6-month period prior to the initiation of SZC

²Optimized RAASi included patients with the same dose or with an up-titration

$\begin{tabular}{ c c c c c c c c c c c c c c c c c c c$		All patients	Optimized RAASi ²	Did not optimize RAASi ³	
Age on index date (years), mean \pm SD62.28 \pm 12.3962.05 \pm 12.3963.13 \pm 12.420.54Female gender, n (%)139 (34.9%)121 (38.5%)18 (21.4%)<0.01*Claims payer, n (%)152 (48.4%)38 (45.2%)0.41Commercial or unknown190 (47.7%)152 (48.4%)38 (45.2%)Medicaid84 (21.1%)69 (22.0%)15 (17.9%)Medicare Advantage124 (31.2%)93 (29.6%)31 (36.9%)Region, n (%)0.950.95Midwest55 (13.8%)44 (14.0%)11 (13.1%)Northeast90 (22.6%)71 (22.6%)19 (22.6%)South150 (37.7%)117 (37.3%)33 (39.3%)West98 (24.6%)77 (24.5%)21 (25.0%)Other5 (1.3%)5 (1.6%)0 (0.0%)HK100Coronorbidities, n (%)0Congestive heart failure87 (21.9%)69 (22.0%)18 (21.4%)Congestive heart failure87 (21.9%)69 (22.0%)18 (21.4%)Congestive heart failure87 (21.9%)69 (22.0%)83 (98.5%)Congestive heart failure87 (21.9%)68 (81.0%)0.58Hypertension387 (97.2%)304 (96.8%)83 (98.8%)0.47Prior Treatment, n (%)HK17 (20.2%)0.44100Loop diuretics176 (44.2%)134 (42.7%)42 (50.0%)0.28Thiazides and thiazide-like diuretics78 (19.6%)51 (19.4%)17 (20.2%)0.44NSAIDs32 (8.0%)27 (8.6%)5 (6.0%)<		(N=398)	(N=314)	(N=84)	p-value
Female gender, n (%)139 (34.9%)121 (38.5%)18 (21.4%)<0.01*Claims payer, n (%)190 (47.7%)152 (48.4%)38 (45.2%)0.41Commercial or unknown190 (47.7%)152 (48.4%)38 (45.2%)0.41Medicare Advantage124 (31.2%)93 (29.6%)31 (36.9%)0.95Midwest55 (13.8%)44 (14.0%)11 (13.1%)0.95Northeast90 (22.6%)71 (22.6%)19 (22.6%)0.95South150 (37.7%)117 (37.3%)33 (39.3%)0.95West98 (24.6%)77 (24.5%)21 (25.0%)0.11Other5 (1.3%)5 (1.6%)0 (0.0%)0.11Congestive heart failure87 (21.9%)69 (22.0%)18 (21.4%)1.00Coronary artery disease110 (27.6%)81 (25.8%)29 (34.5%)0.15Diabetes311 (78.1%)243 (77.4%)68 (81.0%)0.58Hypertension387 (97.2%)304 (96.8%)83 (98.8%)0.47Prior Treatment, n (%)HK treatments73 (18.3%)58 (18.5%)15 (17.9%)1.00Sodium polystyrene sulfonate67 (16.8%)50 (15.9%)17 (20.2%)0.44Loop diuretics176 (44.2%)134 (42.7%)42 (50.0%)0.28Thiazides and thiazide-like diuretics78 (19.6%)61 (19.4%)17 (20.2%)0.99Other treatments176 (44.2%)135 (42.7%)42 (50.0%)0.28Thiazides and thiazide-like diuretics78 (19.6%)61 (19.4%)17 (20.2%) </td <td></td> <td>(2.29 + 12.20)</td> <td>(2.05 + 12.20</td> <td>(2, 12, 10, 10, 10)</td> <td>0.54</td>		(2.29 + 12.20)	(2.05 + 12.20	(2, 12, 10, 10, 10)	0.54
$\begin{tabular}{ c c c c c c c c c c c c c c c c c c c$					
$\begin{array}{c ccccc} \mbox{Commercial or unknown} & 190 (47.7\%) & 152 (48.4\%) & 38 (45.2\%) \\ \mbox{Medicaid} & 84 (21.1\%) & 69 (22.0\%) & 15 (17.9\%) \\ \mbox{Medicare Advantage} & 124 (31.2\%) & 93 (29.6\%) & 31 (36.9\%) \\ \mbox{Region, n} (\%) & 0.95 \\ \mbox{Midwest} & 55 (13.8\%) & 44 (14.0\%) & 11 (13.1\%) \\ \mbox{Northeast} & 90 (22.6\%) & 71 (22.6\%) & 19 (22.6\%) \\ \mbox{South} & 150 (37.7\%) & 117 (37.3\%) & 33 (39.3\%) \\ \mbox{West} & 98 (24.6\%) & 77 (24.5\%) & 21 (25.0\%) \\ \mbox{Other} & 5 (1.3\%) & 5 (1.6\%) & 0 (0.0\%) \\ \mbox{HK} & \\ \mbox{HK} & \\ \mbox{HK diagnosis, n} (\%) & 267 (67.1\%) & 204 (65.0\%) & 63 (75.0\%) & 0.11 \\ \mbox{Comorbidities, n} (\%) & 267 (67.1\%) & 204 (65.0\%) & 63 (75.0\%) & 0.11 \\ \mbox{Coronary artery disease} & 110 (27.6\%) & 81 (25.8\%) & 29 (34.5\%) & 0.15 \\ \mbox{Diabetes} & 311 (78.1\%) & 243 (77.4\%) & 68 (81.0\%) & 0.58 \\ \mbox{Hypertension} & 387 (97.2\%) & 304 (96.8\%) & 83 (98.8\%) & 0.47 \\ \mbox{Prior Treatment, n} (\%) & \\ \mbox{HK treatments} & \\ \mbox{Patiments} & 73 (18.3\%) & 58 (18.5\%) & 15 (17.9\%) & 1.00 \\ \mbox{Sodium polystyrene sulfonate} & 67 (16.8\%) & 50 (15.9\%) & 17 (20.2\%) & 0.44 \\ \mbox{Loop diuretics} & 78 (19.6\%) & 61 (19.4\%) & 17 (20.2\%) & 0.44 \\ \mbox{Loop diuretics} & 239 (60.1\%) & 185 (58.9\%) & 54 (64.3\%) & 0.44 \\ \mbox{NSAIDs} & 32 (8.0\%) & 27 (8.6\%) & 5 (6.0\%) & 0.57 \\ \mbox{All-Cause HRU} & \\ \mbox{Number of inpatient stays, mean \pm SD & 0.40 \pm 0.92 & 0.36 \pm 0.82 & 0.56 \pm 1.20 & 0.13 \\ \end{tabular}$		139 (34.9%)	121 (38.5%)	18 (21.4%)	
Medicaid84 (21.1%)69 (22.0%)15 (17.9%)Medicare Advantage124 (31.2%)93 (29.6%)31 (36.9%)Region, n (%)0.95Midwest55 (13.8%)44 (14.0%)11 (13.1%)Northeast90 (22.6%)71 (22.6%)19 (22.6%)South150 (37.7%)117 (37.3%)33 (39.3%)West98 (24.6%)77 (24.5%)21 (25.0%)Other5 (1.3%)5 (1.6%)0 (0.0%)HK10267 (67.1%)204 (65.0%)63 (75.0%)Congestive heart failure87 (21.9%)69 (22.0%)18 (21.4%)1.00Corronary artery disease110 (27.6%)81 (25.8%)29 (34.5%)0.15Diabetes311 (78.1%)243 (77.4%)68 (81.0%)0.58Hypertension387 (97.2%)304 (96.8%)83 (98.8%)0.47Prior Treatment, n (%)HK134 (42.7%)42 (50.0%)0.28Thiazides and thiazide-like diuretics78 (19.6%)61 (19.4%)17 (20.2%)0.49Other treatments239 (60.1%)185 (58.9%)54 (64.3%)0.44NSAIDs32 (8.0%)27 (8.6%)5 (6.0%)0.57All-Cause HRUAny inpatient stays, mean \pm SD0.40 \pm 0.920.36 \pm 0.820.56 \pm 1.200.13					0.41
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HK diagnosis, n (%) $267 (67.1\%)$ $204 (65.0\%)$ $63 (75.0\%)$ 0.11 Comorbidities, n (%) $87 (21.9\%)$ $69 (22.0\%)$ $18 (21.4\%)$ 1.00 Coronary artery disease $110 (27.6\%)$ $81 (25.8\%)$ $29 (34.5\%)$ 0.15 Diabetes $311 (78.1\%)$ $243 (77.4\%)$ $68 (81.0\%)$ 0.58 Hypertension $387 (97.2\%)$ $304 (96.8\%)$ $83 (98.8\%)$ 0.47 Prior Treatment, n (%)HK treatmentsPatiromer $73 (18.3\%)$ $58 (18.5\%)$ $15 (17.9\%)$ 1.00 Sodium polystyrene sulfonate $67 (16.8\%)$ $50 (15.9\%)$ $17 (20.2\%)$ 0.44 Loop diuretics $176 (44.2\%)$ $134 (42.7\%)$ $42 (50.0\%)$ 0.28 Thiazides and thiazide-like diuretics $78 (19.6\%)$ $61 (19.4\%)$ $17 (20.2\%)$ 0.99 Other treatments $32 (8.0\%)$ $27 (8.6\%)$ $54 (64.3\%)$ 0.44 NSAIDs $32 (8.0\%)$ $27 (8.6\%)$ $5 (6.0\%)$ 0.57 All-Cause HRU $34 (23.6\%)$ $69 (22.0\%)$ $25 (29.8\%)$ 0.18 Number of inpatient stays, mean \pm SD 0.40 ± 0.92 0.36 ± 0.82 0.56 ± 1.20 0.13	Other	5 (1.3%)	5 (1.6%)	0 (0.0%)	
Comorbidities, n (%)87 (21.9%)69 (22.0%)18 (21.4%)1.00Coronary artery disease110 (27.6%)81 (25.8%)29 (34.5%)0.15Diabetes311 (78.1%)243 (77.4%)68 (81.0%)0.58Hypertension387 (97.2%)304 (96.8%)83 (98.8%)0.47Prior Treatment, n (%) </td <td>НК</td> <td></td> <td></td> <td></td> <td></td>	НК				
$\begin{array}{cccc} Congestive heart failure & 87 (21.9\%) & 69 (22.0\%) & 18 (21.4\%) & 1.00 \\ Coronary artery disease & 110 (27.6\%) & 81 (25.8\%) & 29 (34.5\%) & 0.15 \\ Diabetes & 311 (78.1\%) & 243 (77.4\%) & 68 (81.0\%) & 0.58 \\ Hypertension & 387 (97.2\%) & 304 (96.8\%) & 83 (98.8\%) & 0.47 \\ \hline \mathbf{Prior Treatment, n (\%)} & & & & & & & \\ HK treatments & & & & & & & & \\ Patiromer & 73 (18.3\%) & 58 (18.5\%) & 15 (17.9\%) & 1.00 \\ Sodium polystyrene sulfonate & 67 (16.8\%) & 50 (15.9\%) & 17 (20.2\%) & 0.44 \\ Loop diuretics & 176 (44.2\%) & 134 (42.7\%) & 42 (50.0\%) & 0.28 \\ Thiazides and thiazide-like diuretics & 78 (19.6\%) & 61 (19.4\%) & 17 (20.2\%) & 0.99 \\ Other treatments & & & & & & \\ Beta blockers & 239 (60.1\%) & 185 (58.9\%) & 54 (64.3\%) & 0.44 \\ NSAIDs & 32 (8.0\%) & 27 (8.6\%) & 5 (6.0\%) & 0.57 \\ \hline \mathbf{All-Cause HRU} & & & & & & \\ Number of inpatient stays, mean \pm SD & 0.40 \pm 0.92 & 0.36 \pm 0.82 & 0.56 \pm 1.20 & 0.13 \\ \hline \end{array}$	HK diagnosis, n (%)	267 (67.1%)	204 (65.0%)	63 (75.0%)	0.11
$\begin{array}{c} \text{Coronary artery disease} \\ \text{Diabetes} \\ \text{Hypertension} \\ \text{Hypertension} \\ \text{Hypertension} \\ \text{Prior Treatment, n (%)} \\ \text{HK treatments} \\ \text{Patiromer} \\ \text{Sodium polystyrene sulfonate} \\ \text{Loop diuretics} \\ \text{Thiazides and thiazide-like diuretics} \\ \text{Beta blockers} \\ \text{Beta blockers} \\ \text{Beta blockers} \\ \text{Any inpatient stays, n (%)} \\ \text{Mumber of inpatient stays, mean \pm SD \\ \text{SD} \\ \text{SD} \\ \text{O}.40 \pm 0.92 \\ \text{O}.40 \pm 0.92 \\ \text{O}.36 \pm 0.82 \\ \text{O}.46 \pm 0.82 \\ \text{O}.58 \\ \text{SD} \\ \text{O}.58 \\ \text{SD} \\ \text{O}.58 \\ \text{O}.45 \\ \text{O}.58 \\ \text{O}.43 \\ \text{O}.58 \\ \text{O}.43 \\ \text{O}.58 \\ \text{O}.44 \\ \text{O}.58 \\ \text{O}.44 \\ \text{O}.58 \\ \text{O}.44 \\ \text{O}.58 \\ \text{O}.40 \pm 0.92 \\ \text{O}.58 \\ \text{O}.45 \\ \text{O}.58 \\ \text{O}.40 \pm 0.82 \\ \text{O}.56 \pm 1.20 \\ \text{O}.58 \\ \text{O}.15 \\ \text{O}.58 \\ \text{O}.40 \pm 0.92 \\ \text{O}.56 \pm 0.82 \\ \text{O}.56 \pm 1.20 \\ \text{O}.56 \\ \text{O}.57 \\ \text{O}.55 \\ \text{O}.15 \\ \text{O}.55 \\ \text{O}.55 \\ \text{O}.55 \\ \text{O}.15 \\ \text{O}.55 \\ \text{O}.15 \\ \text{O}.55 \\ \text{O}.55 \\ \text{O}.55 \\ \text{O}.15 \\ \text{O}.55 \\ \text{O}.55 \\ \text{O}.55 \\ \text{O}.55 \\ \text{O}.15 \\ \text{O}.55 \\ \text{O}.55 \\ \text{O}.55 \\ \text{O}.15 \\ \text{O}.55 \\ \text{O}.55 \\ \text{O}.55 \\ \text{O}.15 \\ \text{O}.55 \\ \text{O}.55 \\ \text{O}.15 \\ \text{O}.55 \\ \text{O}.15 \\ \text{O}.55 \\ \text{O}.15 \\ \text{O}.55 \\ \text{O}.55 \\ \text{O}.55 \\ \text{O}.55 \\ \text{O}.15 \\ \text{O}.55 \\ \text{O}.15 \\ \text{O}.55 \\ \text{O}.55 \\ \text{O}.55 \\ \text{O}.55 \\ \text{O}.55 \\ \text{O}.55 \\$	Comorbidities, n (%)				
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Congestive heart failure	87 (21.9%)	69 (22.0%)	18 (21.4%)	1.00
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Coronary artery disease	110 (27.6%)	81 (25.8%)	29 (34.5%)	0.15
Hypertension $387 (97.2\%)$ $304 (96.8\%)$ $83 (98.8\%)$ 0.47 Prior Treatment, n (%)HK treatments $73 (18.3\%)$ $58 (18.5\%)$ $15 (17.9\%)$ 1.00 Sodium polystyrene sulfonate $67 (16.8\%)$ $50 (15.9\%)$ $17 (20.2\%)$ 0.44 Loop diuretics $176 (44.2\%)$ $134 (42.7\%)$ $42 (50.0\%)$ 0.28 Thiazides and thiazide-like diuretics $78 (19.6\%)$ $61 (19.4\%)$ $17 (20.2\%)$ 0.99 Other treatments $239 (60.1\%)$ $185 (58.9\%)$ $54 (64.3\%)$ 0.44 NSAIDs $32 (8.0\%)$ $27 (8.6\%)$ $5 (6.0\%)$ 0.57 All-Cause HRU $94 (23.6\%)$ $69 (22.0\%)$ $25 (29.8\%)$ 0.18 Number of inpatient stays, mean \pm SD 0.40 ± 0.92 0.36 ± 0.82 0.56 ± 1.20 0.13		311 (78.1%)	243 (77.4%)	68 (81.0%)	0.58
Prior Treatment, n (%)HK treatmentsPatiromer73 (18.3%)58 (18.5%)15 (17.9%)1.00Sodium polystyrene sulfonate67 (16.8%)50 (15.9%)17 (20.2%)0.44Loop diuretics176 (44.2%)134 (42.7%)42 (50.0%)0.28Thiazides and thiazide-like diuretics78 (19.6%)61 (19.4%)17 (20.2%)0.99Other treatmentsBeta blockers239 (60.1%)185 (58.9%)54 (64.3%)0.44NSAIDs32 (8.0%)27 (8.6%)5 (6.0%)0.57All-Cause HRUAny inpatient stays, n (%)94 (23.6%)69 (22.0%)25 (29.8%)0.18Number of inpatient stays, mean \pm SD0.40 \pm 0.920.36 \pm 0.820.56 \pm 1.200.13	Hypertension	387 (97.2%)	304 (96.8%)	83 (98.8%)	0.47
HK treatments73 (18.3%)58 (18.5%)15 (17.9%)1.00Sodium polystyrene sulfonate67 (16.8%)50 (15.9%)17 (20.2%)0.44Loop diuretics176 (44.2%)134 (42.7%)42 (50.0%)0.28Thiazides and thiazide-like diuretics78 (19.6%)61 (19.4%)17 (20.2%)0.99Other treatments239 (60.1%)185 (58.9%)54 (64.3%)0.44NSAIDs32 (8.0%)27 (8.6%)5 (6.0%)0.57All-Cause HRU94 (23.6%)69 (22.0%)25 (29.8%)0.18Number of inpatient stays, mean \pm SD0.40 \pm 0.920.36 \pm 0.820.56 \pm 1.200.13		· · · ·		· · · · ·	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$					
Sodium polystyrene sulfonate Loop diuretics $67 (16.8\%)$ $176 (44.2\%)$ $50 (15.9\%)$ $134 (42.7\%)$ $17 (20.2\%)$ $42 (50.0\%)$ 0.44 0.28 0.28 Thiazides and thiazide-like diureticsThiazides and thiazide-like diuretics $78 (19.6\%)$ $61 (19.4\%)$ $17 (20.2\%)$ 0.99 Other treatments $239 (60.1\%)$ $185 (58.9\%)$ $54 (64.3\%)$ 0.44 0.57 NSAIDs $32 (8.0\%)$ $27 (8.6\%)$ $5 (6.0\%)$ 0.57 All-Cause HRU $94 (23.6\%)$ $69 (22.0\%)$ $25 (29.8\%)$ 0.18 0.18 Number of inpatient stays, mean \pm SD 0.40 ± 0.92 0.36 ± 0.82 0.56 ± 1.20 0.13		73 (18.3%)	58 (18.5%)	15 (17.9%)	1.00
Loop diuretics $176 (44.2\%)$ $134 (42.7\%)$ $42 (50.0\%)$ 0.28 Thiazides and thiazide-like diuretics $78 (19.6\%)$ $61 (19.4\%)$ $17 (20.2\%)$ 0.99 Other treatments $239 (60.1\%)$ $185 (58.9\%)$ $54 (64.3\%)$ 0.44 NSAIDs $32 (8.0\%)$ $27 (8.6\%)$ $5 (6.0\%)$ 0.57 All-Cause HRU $42 (23.6\%)$ $69 (22.0\%)$ $25 (29.8\%)$ 0.18 Number of inpatient stays, mean \pm SD 0.40 ± 0.92 0.36 ± 0.82 0.56 ± 1.20 0.13	Sodium polystyrene sulfonate	· · · · · ·	· /	· · · · · ·	0.44
Thiazides and thiazide-like diuretics $78 (19.6\%)$ $61 (19.4\%)$ $17 (20.2\%)$ 0.99 Other treatments $239 (60.1\%)$ $185 (58.9\%)$ $54 (64.3\%)$ 0.44 NSAIDs $32 (8.0\%)$ $27 (8.6\%)$ $5 (6.0\%)$ 0.57 All-Cause HRU 4123.6% $94 (23.6\%)$ $69 (22.0\%)$ $25 (29.8\%)$ 0.18 Number of inpatient stays, mean \pm SD 0.40 ± 0.92 0.36 ± 0.82 0.56 ± 1.20 0.13		· · · · · ·	· /		
Other treatments $239 (60.1\%)$ $185 (58.9\%)$ $54 (64.3\%)$ 0.44 NSAIDs $32 (8.0\%)$ $27 (8.6\%)$ $5 (6.0\%)$ 0.57 All-Cause HRU $94 (23.6\%)$ $69 (22.0\%)$ $25 (29.8\%)$ 0.18 Number of inpatient stays, mean \pm SD 0.40 ± 0.92 0.36 ± 0.82 0.56 ± 1.20 0.13		· · · ·	· · · · · ·	· · · · · ·	
Beta blockers $239 (60.1\%)$ $185 (58.9\%)$ $54 (64.3\%)$ 0.44 NSAIDs $32 (8.0\%)$ $27 (8.6\%)$ $5 (6.0\%)$ 0.57 All-Cause HRU $94 (23.6\%)$ $69 (22.0\%)$ $25 (29.8\%)$ 0.18 Number of inpatient stays, mean \pm SD 0.40 ± 0.92 0.36 ± 0.82 0.56 ± 1.20 0.13					
NSAIDs $32 (8.0\%)$ $27 (8.6\%)$ $5 (6.0\%)$ 0.57 All-Cause HRU94 (23.6\%) $69 (22.0\%)$ $25 (29.8\%)$ 0.18 Any inpatient stays, n (%) $94 (23.6\%)$ 0.36 ± 0.82 0.56 ± 1.20 0.13		239 (60 1%)	185 (58 9%)	54 (64 3%)	0 44
All-Cause HRU94 (23.6%)69 (22.0%)25 (29.8%)0.18Any inpatient stays, n (%)94 (23.6%) 0.40 ± 0.92 0.36 ± 0.82 0.56 ± 1.20 0.13		· · · ·	· · · · · ·		
Any inpatient stays, n (%) $94 (23.6\%)$ $69 (22.0\%)$ $25 (29.8\%)$ 0.18 Number of inpatient stays, mean \pm SD 0.40 ± 0.92 0.36 ± 0.82 0.56 ± 1.20 0.13		32 (0.070)	27 (0.070)	5 (0.070)	0.07
Number of inpatient stays, mean \pm SD 0.40 ± 0.92 0.36 ± 0.82 0.56 ± 1.20 0.13		94(23.6%)	69(22.0%)	25 (29.8%)	0.18
		· · · · ·	· /	· · · · · ·	
	Any ED visits, n (%)	115 (28.9%)	83 (26.4%)	32 (38.1%)	0.15
Any ED visits, $n(\pi)$ $n(\pi)$ $n(\pi)$ $n(\pi)$ $n(\pi)$ $n(\pi)$ $n(\pi)$ $n(\pi)$ Number of ED visits, mean \pm SD 0.44 ± 0.91 0.40 ± 0.89 0.61 ± 0.98 $< 0.05^*$		· · · ·	· /	· · · · · ·	
Any outpatient visits, $n(\%)$ 0.44 ± 0.91 0.40 ± 0.89 0.01 ± 0.98 < 0.05 Any outpatient visits, $n(\%)$ $392 (98.5\%)$ $310 (98.7\%)$ $82 (97.6\%)$ 0.61	· · · · · · · · · · · · · · · · · · ·				
Number of outpatient visits, mean \pm SD 14.56 \pm 15.01 13.89 \pm 13.62 17.04 \pm 19.23 0.13	• •	. ,			

Supplemental Table 3. Baseline Characteristics of Patients With CKD Initiating SZC¹

Abbreviations: CKD, chronic kidney disease; ED, emergency department; ESKD, end-stage kidney disease; HK, hyperkalemia; HRU, healthcare resource utilization; NSAID, non-steroidal anti-inflammatory drug; SD, standard deviation; SZC, sodium zirconium cyclosilicate

¹Baseline was the 6-month period prior to the initiation of SZC

²Optimized RAASi included patients with the same dose or with an up-titration

	All patients (N=311)	Optimized RAASi ² (N=243)	Did not optimize RAASi ³ (N=68)	p-value
Demographics	(11-011)	(11-210)	(11-00)	p vulue
Age on index date (years), mean \pm SD	62.69 ± 11.77	62.73 ± 11.66	62.54 ± 12.23	0.95
Female gender, n (%)	110 (35.4%)	96 (39.5%)	14 (20.6%)	< 0.01*
Claims payer, n (%)				0.62
Commercial or unknown	139 (44.7%)	109 (44.9%)	30 (44.1%)	
Medicaid	66 (21.2%)	54 (22.2%)	12 (17.6%)	
Medicare Advantage	106 (34.1%)	80 (32.9%)	26 (38.2%)	
Region, n (%)				0.95
Midwest	41 (13.2%)	33 (13.6%)	8 (11.8%)	
Northeast	71 (22.8%)	54 (22.2%)	17 (25.0%)	
South	114 (36.7%)	89 (36.6%)	25 (36.8%)	
West	81 (26.0%)	63 (25.9%)	18 (26.5%)	
Other	4 (1.3%)	4 (1.6%)	0 (0.0%)	
НК			× /	
HK diagnosis, n (%)	210 (67.5%)	161 (66.3%)	49 (72.1%)	0.45
Comorbidities, n (%)	× ,			
Congestive heart failure	75 (24.1%)	60 (24.7%)	15 (22.1%)	0.77
Coronary artery disease	94 (30.2%)	70 (28.8%)	24 (35.3%)	0.38
Hypertension	307 (98.7%)	239 (98.4%)	68 (100.0%)	0.58
Prior Treatment, n (%)	× ,			
HK treatments				
Patiromer	52 (16.7%)	40 (16.5%)	12 (17.6%)	0.96
Sodium polystyrene sulfonate	50 (16.1%)	37 (15.2%)	13 (19.1%)	0.56
Loop diuretics	150 (48.2%)	114 (46.9%)	36 (52.9%)	0.46
Thiazides and thiazide-like diuretics	69 (22.2%)	55 (22.6%)	14 (20.6%)	0.85
Other treatments				
Beta blockers	197 (63.3%)	151 (62.1%)	46 (67.6%)	0.49
NSAIDs	27 (8.7%)	25 (10.3%)	2 (2.9%)	0.08
All-Cause HRU				
Any inpatient stays, n (%)	81 (26.0%)	61 (25.1%)	20 (29.4%)	0.58
Number of inpatient stays, mean \pm SD	0.44 ± 0.95	0.41 ± 0.87	0.56 ± 1.19	0.42
Any ED visits, n (%)	92 (29.6%)	67 (27.6%)	25 (36.8%)	0.19
Number of ED visits, mean \pm SD	0.48 ± 0.99	0.44 ± 0.98	0.62 ± 1.04	0.13
Any outpatient visits, n (%)	305 (98.1%)	239 (98.4%)	66 (97.1%)	0.62
Number of outpatient visits, mean \pm SD	15.46 ± 16.24	14.94 ± 14.87	17.34 ± 20.44	0.54

Supplemental Table 4. Baseline Characteristics of Patients With CKD + Diabetes Initiating SZC¹

Abbreviations: CKD, chronic kidney disease; ED, emergency department; ESKD, end-stage kidney disease; HK, hyperkalemia; HRU, healthcare resource utilization; NSAID, non-steroidal anti-inflammatory drug; SD, standard deviation; SZC, sodium zirconium cyclosilicate

¹Baseline was the 6-month period prior to the initiation of SZC

²Optimized RAASi included patients with the same dose or with an up-titration

	A	ll patients with	nout ESKD	All patients with stage 3-5 CKD			All patients with stage 3-5 CKD + Diabetes					
	All patients (N=472)	Optimized RAASi ² (N=370)	Did not optimize RAASi ³ (N=102)	p- value	All patients (N=398)	Optimized RAASi ² (N=314)	Did not optimize RAASi ³ (N=84)	p- value	All patients (N=311)	Optimized RAASi ² (N=243)	Did not optimize RAASi ³ (N=68)	p- value
RAASi	444	349	95	0.83	375	297	78	0.73	293	228	65	0.77
	(94.1%)	(94.3%)	(93.1%)		(94.2%)	(94.6%)	(92.9%)		(94.2%)	(93.8%)	(95.6%)	
ACEi	245	192	53	1.00	214	167	47	0.74	164	124	40	0.32
	(51.9%)	(51.9%)	(52.0%)		(53.8%)	(53.2%)	(56.0%)		(52.7%)	(51.0%)	(58.8%)	
ARB	189	150	39	0.76	154	125	29	0.45	123	100	23	0.34
	(40.0%)	(40.5%)	(38.2%)		(38.7%)	(39.8%)	(34.5%)		(39.5%)	(41.2%)	(33.8%)	
ARNI	19 (4.0%)	15 (4.1%)	4 (3.9%)	1.00	12 (3.0%)	9 (2.9%)	3 (3.6%)	0.72	11 (3.5%)	8 (3.3%)	3 (4.4%)	0.71
DRI	1 (0.2%)	1 (0.3%)	0 (0.0%)	1.00	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
MRA	59			0.45	46			0.64	35			0.35
	(12.5%)	49 (13.2%)	10 (9.8%)		(11.6%)	38 (12.1%)	8 (9.5%)		(11.3%)	30 (12.3%)	5 (7.4%)	

Supplemental Table 5. RAASi Therapy at Initiation of SZC¹ Among Patients Without ESKD, With CKD, and With CKD + Diabetes

Abbreviations: ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; CKD, chronic kidney disease; DRI, direct renin inhibitor; ESKD, end-stage kidney disease MRA, mineralocorticoid receptor antagonist, RAASi, renin-angiotensin-aldosterone system inhibitor; RAASi, renin-angiotensin system inhibitor

¹Patients could be taking monotherapy or combination therapy so the percentages may not add to 100%

²Optimized RAASi included patients with the same dose or with an up-titration