PASS INFORMATION

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Research Question and Objectives	The primary objective is to characterize the treatment and management of hypocalcemia among a retrospective cohort of European hemodialysis patients with secondary hyperparathyroidism receiving cinacalcet
Country(ies) of Study	Czech Republic, France, Hungary, Ireland, Italy, Poland, Portugal, Romania, Russia, Serbia, Slovak Republic, Slovenia, Spain, Turkey, and the United Kingdom
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1. Abstract

- **Title**

Characterizing the Management of Hypocalcemia Among European Hemodialysis Patients Receiving Cinacalcet

- **Keywords**

Calcimimetic, cinacalcet, hemodialysis, hypocalcemia, secondary hyperparathyroidsim

- **Rationale and Background**

Hypocalcemia is a common adverse event in hemodialysis (HD) patients with secondary hyperparathyroidism (SHPT) receiving cinacalcet as treatment. Consequently, this can affect a patient's level of medication adherence and control of SHPT. The objective of the study was to characterize clinician and management practices of hypocalcemia in an incident European HD patient cohort with SHPT who were prescribed cinacalcet.

- **Research Question and Objectives**

The primary objective is to characterize the treatment and management of hypocalcemia among a retrospective cohort of European hemodialysis patients with secondary hyperparathyroidism receiving cinacalcet.

The secondary objectives were

- to investigate the incidence and predictors of hypocalcemia
- to investigate the rate of re-initiation and predictors of cinacalcet re-initiation among HD patients who discontinued cinacalcet following hypocalcemia

- **Study Design**

A retrospective cohort study using electronic medical records of HD patients prescribed cinacalcet in Europe

- **Setting**

The study was conducted in a retrospective cohort (ARO-2) of adult chronic disease patients receiving hemodialysis and enrolled between 1 January 2007 and 31 December 2009 at one of the Euorpean Fresenius Medical Care (FMC) facility in participating countries (*Czech Republic, France, Hungary, Ireland, Italy, Poland, Portugal, Romania, Russia, Serbia, Slovak Republic, Slovenia, Spain, and United Kingdom*) and Turkey.

- **Subjects and Study Size, Including Dropouts**

Subjects were eligible if they were aged ≥18, filled a cinacalcet prescriptioin after 01 January 2007, enrolled in ARO-2 for at least 90 days prior to cinacalcet initiation and have at least 90 days of follow-up following cinacalcet initiation. Patients with a history of parathyroidectomy up to and including the first 90 days of follow-up, had a prescription for cinacalcet for less than 15 days with no further prescriptions were excluded.

HD patients who had a serum Ca >2.1 mmol/L at time of cinacalcet initation was included in the primary analysis.

- **Variables and Data Sources**

Outcome Variables: Incidence of hypocalcemia; frequency of hypocalcemia; time to first hypocalcemia event; time to any treatment intervention, rate of cinacalcet discontinuation; cinacalcet prescribing patterns; prescribing patterns for vitamin D, phosphate binders and CVD medications; time to cinacalcet re-initiation following discontinuation, rate of cinacalcet re-initation; kinetics of hypocalcemia; and serum calcium levels.

Exposure Variable: cinacalcet initation, development of hypocalcemia, and cinacalcet discontinuation

Other Covariates: Demographic (age, gender, country, exposure pre-KDIGO); clinical (hospitalization, BMI, pre-dialysis systolic blood pressure, smoking status); medical history (CKD aetiology); medical events (diabetes, cancer, CVD, fracture); dialysis parameters (vascular access, dialysis vintage, calcium dialysate concentration, net ultrafiltration, actual blood flow); laboratory parameters (hemoglobin, ferritin, CRP, serum albumin, creatinine, total calcium, phosphate, alkaline phosphatase, parathyroid hormone (PTH)); and medication use (cinacalcet, paricalcitol, other active vitamin D (AVD), phosphate binder, and cardiovascular medication)

- **Results**

In this retrospective cohort of 905 HD subjects with a cincalcet prescription and normal Ca, 610 (72%) subjects developed hypocalcemia within 12 months of treatment

initiation. Among these subjects, 68% had mild, 23.1% had moderate and 8.9% had severe hypocalcemia (**Table 1**). Subjects with severe hypocalcemia had a higher baseline PTH compared to those mild and moderate hypocalcemia. Median time to hypocalcemia event was 4 months. Having no cathetar access, low albumin, and high PTH were predictors of hypocalcemia; whereas residing in Western Europe compared to the Iberian Peninsula and low hemoglobin appeared to reduce the risk of hypocalcemia. Regardless of severity, the majority of subjects had a persistent cinacalcet prescription at 12 months following hypocalcemia event, overall (69%) and by severity of mild (71%), moderate (69%) and severe (56%) (**Table 2**). Median Ca levels for hypocalcemia subjects with persistent cinicalcet prescription returned to normal (>2.1 mmol/L) in the first month following the event and remained stable within the normal range in the subsequent months.

Generally, there was no treatment intervention for calcitriol/afacalidiol, paricalcitol, calcium-based phosphate binder, and dialysate calcium use prior to or at time of cinacalcet initiation regardless of whether subjects developed or did not develop hypocalcemia (**Table 3**). In the 30 days following hypocalcemia, generally, there was no change in treatment. Dose remained stable for 78.5% of cinacalcet, 73.4% of calcitriol/alfaccalcidol, 64.8% of paricalcitol, 80.8% of calcim-based phosphate binder users. Dialysate calcium dose was also stable for 83.6% of users. Similar trends were found by severity of hypocalcemia (**Table 4**).

Overall, within 30 days of hypocalcemia event, 38.9% had an intervention that included discontinuation or reduced dose of cinacalcet, increased dialysate calcium, or initiated/up-titrated calcitriol/alfacalcidol, paricalcitol, or calcium-based phosphate binder. Specifically, cinacalcet was discontinued or had their dose reduced in 11.7% of subjects; calcitriol/alfacalcidol was initiated or up-titrated in 6.2% of subjects; paricalcitol was initiated or up-titrated in 12.6% of subjects, and calcium-based phosphate binders was initiated or up-titrated in 6.2% and dialysate calcium was increased for 11.3% of subjects (**Table 4**).

- **Discussion**
  - Hypocalcemia is common among cinacalcet users. Cinacalcet-induced hypocalcemia appear to be tolerated within this European observational cohort of incident HD patients prescribed cinacalcet. The results suggest that the benefit of cinacalcet to manage SHPT can be manged with the risk of hypocalcemia.

Table 1. Demographic and clinical history characteristics of subjects who do not develop hypocalcemia vs. patients who develop hypocalcemia within 12 months following cinacalcet treatment initiation

Baseline characteristics	Overall no. of patients who did not develop hypocalcemia within 12 months (N=295)	Overall no. of patients who develop hypocalcemia within 12 months (N=610)	Subjects who develop hypocalcemia within 12 months (N=610)		
			Mild ≥2.0-<2.1 mmol/L (N=415)	Moderate ≥1.87-<2.0 mmol/L (N=141)	Severe <1.87 mmol/L (N=54)
Patient Age Category, No. (%)					
18-44	39 (13.2)	80 (13.1)	56 (13.5)	20 (14.2)	4 (7.4)
45-54	37 (12.5)	76 (12.5)	54 (13.0)	14 (9.9)	8 (14.8)
55-64	58 (19.7)	115 (18.9)	75 (18.1)	29 (20.6)	11 (20.4)
65-74	79 (26.8)	152 (24.9)	101 (24.3)	40 (28.4)	11 (20.4)
75+	82 (27.8)	187 (30.7)	129 (31.1)	38 (27.0)	20 (37.0)
Gender, No. (%)					
Male	173 (58.6)	352 (57.7)	240 (57.8)	82 (58.2)	30 (55.6)
Female	122 (41.4)	257 (42.1)	175 (42.2)	59 (41.8)	23 (42.6)
Missing	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.9)
Geographical area[a], No. (%)					
Eastern Europe	25 (8.5)	56 (9.2)	38 (9.2)	15 (10.6)	3 (5.6)
Western Europe	33 (11.2)	41 (6.7)	28 (6.7)	8 (5.7)	5 (9.3)
Iberian peninsula	237 (80.3)	513 (84.1)	349 (84.1)	118 (83.7)	46 (85.2)
Period pre-KDIGO[b], No. (%)					
Yes	65 (22.0)	134 (22.0)	88 (21.2)	32 (22.7)	14 (25.9)
No	230 (78.0)	476 (78.0)	327 (78.8)	109 (77.3)	40 (74.1)
Smoking status, No. (%)					
Current	32 (10.8)	64 (10.5)	44 (10.6)	15 (10.6)	5 (9.3)
Former	48 (16.3)	90 (14.8)	63 (15.2)	20 (14.2)	7 (13.0)

Non-smoker	110 (37.3)	206 (33.8)	140 (33.7)	46 (32.6)	20 (37.0)
Missing	105 (35.6)	250 (41.0)	168 (40.5)	60 (42.6)	22 (40.7)
BMI (kg/m2), No. (%)					
<18.5	4 (1.4)	7 (1.1)	6 (1.4)	1 (0.7)	0 (0.0)
≥18.5 - <25	79 (26.8)	162 (26.6)	115 (27.7)	37 (26.2)	10 (18.5)
≥25 - <30	101 (34.2)	232 (38.0)	154 (37.1)	54 (38.3)	24 (44.4)
>=30	75 (25.4)	148 (24.3)	102 (24.6)	35 (24.8)	11 (20.4)
Missing	36 (12.2)	61 (10.0)	38 (9.2)	14 (9.9)	9 (16.7)
Blood pressure (mmHg), No. (%)					
<120	70 (23.7)	130 (21.3)	95 (22.9)	24 (17.0)	11 (20.4)
>=120 - <130	50 (16.9)	105 (17.2)	69 (16.6)	27 (19.1)	9 (16.7)
>=130 - <140	48 (16.3)	105 (17.2)	74 (17.8)	22 (15.6)	9 (16.7)
>=140 - <160	79 (26.8)	157 (25.7)	98 (23.6)	41 (29.1)	18 (33.3)
>=160	48 (16.3)	113 (18.5)	79 (19.0)	27 (19.1)	7 (13.0)
Clinical history, No. (%)					
Hospitalisation	137 (46.4)	310 (50.8)	207 (49.9)	71 (50.4)	32 (59.3)
Diabetes	89 (30.2)	194 (31.8)	128 (30.8)	46 (32.6)	20 (37.0)
Cancer	26 (8.8)	59 (9.7)	42 (10.1)	11 (7.8)	6 (11.1)
Cardiovascular disease	131 (44.4)	304 (49.8)	199 (48.0)	77 (54.6)	28 (51.9)
Fracture	14 (4.7)	29 (4.8)	21 (5.1)	6 (4.3)	2 (3.7)
CKD aetiology, No. (%)					
Hypertension / vascular	55 (18.6)	113 (18.5)	78 (18.8)	25 (17.7)	10 (18.5)
Glomerulonephritis	35 (11.9)	75 (12.3)	52 (12.5)	19 (13.5)	4 (7.4)
Diabetic Nephropathy	63 (21.4)	109 (17.9)	69 (16.6)	29 (20.6)	11 (20.4)
Tubulo-interstitial	36 (12.2)	71 (11.6)	45 (10.8)	21 (14.9)	5 (9.3)
Polycystic Kidney Disease	18 (6.1)	43 (7.0)	26 (6.3)	11 (7.8)	6 (11.1)
Other	85 (28.8)	196 (32.1)	143 (34.5)	35 (24.8)	18 (33.3)
Missing/Invalid	3 (1.0)	3 (0.5)	2 (0.5)	1 (0.7)	0 (0.0)

BMI, body mass index; CKD, chronic kidney disease

[a] Eastern Europe (Czech Republic, Hugnary, Poland, Romania, Russia, Serbia, Slovak Republic, Slovenia, and Turkey); Western Europe (Frane, Ireland, Italy, and United Kingdom); Iberian Peninsula (Portugal and Spain)

[b] Pre-KDIGO: Kidney Disease: Improving Global Outcomes CKD-MBD Work Group publication (01 August 2009).

Table 2. Cinacalcet persistence following hypocalcaemia event by calcium at hypocalcaemia event

	Overall (N=610)	**Mild** 2.0 ≤ Ca < 2.1 mmol/L (N=415)	**Moderate** 1.87 ≤ Ca < 2.0 mmol/L (N=141)
1 month following treatment initiation			
Patient Status			
Number of patients	610	415	141
Discontinuation (after 1st hypocalcaemia event) - n (%)	9 (1.5)	8 (1.9)	0 (0.0)
Censored - n (%)	601 (98.5)	407 (98.1)	141 (100.0)
KM persistence probability	0.99	0.98	1
95% CI	(0.97, 0.99)	(0.97, 0.99)	(1.00, 1.00)
2 months following treatment initiation			
Patient Status			
Number of patients	594	401	141
Discontinuation (after 1st hypocalcaemia event) - n (%)	10 (1.7)	9 (2.2)	1 (0.7)
Censored - n (%)	584 (98.3)	392 (97.8)	140 (99.3)
KM persistence probability	0.97	0.96	0.99
95% CI	(0.95, 0.98)	(0.94, 0.98)	(0.97, 1.00)
3 months following treatment initiation			
Patient Status			
Number of patients	575	385	138
Discontinuation (after 1st hypocalcaemia event) - n (%)	23 (4.0)	16 (4.2)	3 (2.2)
Censored - n (%)	552 (96.0)	369 (95.8)	135 (97.8)
KM persistence probability	0.93	0.92	0.97
95% CI	(0.91, 0.95)	(0.89, 0.94)	(0.94, 0.99)
4 months following treatment initiation			
Patient Status			
Number of patients	541	360	134
Discontinuation (after 1st hypocalcaemia event) - n (%)	24 (4.4)	11 (3.1)	11 (8.2)

Censored - n (%)	517 (95.6)	349 (96.9)	123 (91.8)
KM persistence probability	0.89	0.89	0.89
95% CI	(0.86, 0.91)	(0.86, 0.92)	(0.83, 0.94)
5 months following treatment initiation			
Patient Status			
Number of patients	501	336	120
Discontinuation (after 1st hypocalcaemia event) - n (%)	11 (2.2)	8 (2.4)	2 (1.7)
Censored - n (%)	490 (97.8)	328 (97.6)	118 (98.3)
KM persistence probability	0.87	0.87	0.88
95% CI	(0.84, 0.90)	(0.83, 0.90)	(0.82, 0.93)
6 months following treatment initiation			
Patient Status			
Number of patients	480	322	115
Discontinuation (after 1st hypocalcaemia event) - n (%)	19 (4.0)	7 (2.2)	6 (5.2)
Censored - n (%)	461 (96.0)	315 (97.8)	109 (94.8)
KM persistence probability	0.83	0.85	0.83
95% CI	(0.80, 0.86)	(0.81, 0.88)	(0.76, 0.89)
7 months following treatment initiation			
Patient Status			
Number of patients	449	307	106
Discontinuation (after 1st hypocalcaemia event) - n (%)	25 (5.6)	17 (5.5)	5 (4.7)
Censored - n (%)	424 (94.4)	290 (94.5)	101 (95.3)
KM persistence probability	0.79	0.8	0.79
95% CI	(0.75, 0.82)	(0.76, 0.84)	(0.72, 0.86)
8 months following treatment initiation			
Patient Status			
Number of patients	416	285	100
Discontinuation (after 1st hypocalcaemia event) - n (%)	15 (3.6)	8 (2.8)	4 (4.0)
Censored - n (%)	401 (96.4)	277 (97.2)	96 (96.0)
KM persistence probability	0.76	0.78	0.76

95% CI	(0.72, 0.79)	(0.74, 0.82)	(0.68, 0.83)
9 months following treatment initiation			
Patient Status			
Number of patients	392	270	94
Discontinuation (after 1st hypocalcaemia event) - n (%)	11 (2.8)	7 (2.6)	3 (3.2)
Censored - n (%)	381 (97.2)	263 (97.4)	91 (96.8)
KM persistence probability	0.74	0.76	0.74
95% CI	(0.70, 0.77)	(0.72, 0.80)	(0.66, 0.81)
10 months following treatment initiation			
Patient Status			
Number of patients	373	258	90
Discontinuation (after 1st hypocalcaemia event) - n (%)	2 (0.5)	0 (0.0)	2 (2.2)
Censored - n (%)	371 (99.5)	258 (100.0)	88 (97.8)
KM persistence probability	0.73	0.76	0.72
95% CI	(0.70, 0.77)	(0.72, 0.80)	(0.64, 0.79)
11 months following treatment initiation			
Patient Status			
Number of patients	363	253	86
Discontinuation (after 1st hypocalcaemia event) - n (%)	12 (3.3)	11 (4.3)	0 (0.0)
Censored - n (%)	351 (96.7)	242 (95.7)	86 (100.0)
KM persistence probability	0.71	0.73	0.72
95% CI	(0.67, 0.75)	(0.68, 0.77)	(0.64, 0.79)
12 months following treatment initiation			
Patient Status			
Number of patients	337	234	81
Discontinuation (after 1st hypocalcaemia event) - n (%)	10 (3.0)	7 (3.0)	3 (3.7)
Censored - n (%)	327 (97.0)	227 (97.0)	78 (96.3)
KM persistence probability (96% CI)	0.69 (0.65, 0.73)	0.71 (0.66, 0.75)	0.69 (0.61, 0.77)

Table 3. Treatment characteristics of haemodialysis patients prior to and at time of cinacalcet initiation among subjects who developed and did not develop hypocalcemia

Treatment prior to or at time of cinacalcet initation	No hypocalcaemia within 12 months N=295	Patients with a hypocalcaemia within 12 months of initiation			
			Ca at time of hypocalcaemia		
		Overall N=610	Ca ≥2.00 - <2.10 mmol/L N=415	Ca≥1.87 - <2.00 mmol/L N=141	Ca <1.87 mmol/L N=54
Cinacalcet					
Average daily dose (mg/day), median (Q1, Q3)	30.0 (12.9, 30.0)	30.0 (17.1, 30.0)	30.0 (17.1, 30.0)	30.0 (17.1, 30.0)	30.0 (30.0, 30.0)
Calcitriol/Alfacalcidol					
Use, n (%)	60 (20.3)	130 (21.3)	88 (21.2)	34 (24.1)	8 (14.8)
Average daily dose (µg/day), median (Q1, Q3)	0.4 (0.2, 0.5)	0.3 (0.2, 0.4)	0.3 (0.2, 0.4)	0.3 (0.3, 0.4)	0.3 (0.3, 0.5)
New users, n (%)	2 (3.3)	4 (3.1)	2 (2.3)	2 (5.9)	0 (0.0)
Continuing users, n (%)	58 (96.7)	126 (96.9)	86 (97.7)	32 (94.1)	8 (100.0)
Stable dose, n (%)	47 (81.0)	106 (84.1)	72 (83.7)	26 (81.3)	8 (100.0)
Up-titration, n (%)	7 (12.1)	9 (7.1)	6 (7.0)	3 (9.4)	0 (0.0)
Down-titration, n (%)	4 (6.9)	11 (8.7)	8 (9.3)	3 (9.4)	0 (0.0)
Paricalcitol					
Use, n (%)	113 (38.3)	234 (38.4)	164 (39.5)	52 (36.9)	18 (33.3)
Average daily dose (µg/day), median (Q1, Q3)	0.9 (0.6, 1.4)	0.9 (0.6, 1.2)	0.9 (0.6, 1.1)	0.9 (0.7, 1.5)	0.8 (0.4, 1.4)
New users, n (%)	2 (1.8)	17 (7.3)	12 (7.3)	3 (5.8)	2 (11.1)
Continuing users, n (%)	111 (98.2)	217 (92.7)	152 (92.7)	49 (94.2)	16 (88.9)
Stable dose, n (%)	78 (70.3)	164 (75.6)	113 (74.3)	39 (79.6)	12 (75.0)
Up-titration, n (%)	23 (20.7)	26 (12.0)	18 (11.8)	6 (12.2)	2 (12.5)
Down-titration, n (%)	10 (9.0)	27 (12.4)	21 (13.8)	4 (8.2)	2 (12.5)
Calcium-based phosphate binder					
Use, n (%)	64 (21.7)	140 (23.0)	93 (22.4)	36 (25.5)	11 (20.4)
Average daily dose (mg/day), median (Q1, Q3)	1942.5 (714.5, 2820.0)	1980.0 (1143.0, 3150.0)	1980.0 (1143.0, 3300.0)	2040.0 (918.8, 3960.0)	1980.0 (660.0, 2000.0)
New users, n (%)	1 (1.6)	6 (4.3)	4 (4.3)	2 (5.6)	0 (0.0)
Continuing users, n (%)	63 (98.4)	134 (95.7)	89 (95.7)	34 (94.4)	11 (100.0)

Stable dose, n (%)	56 (88.9)	120 (89.6)	77 (86.5)	32 (94.1)	11 (100.0)
Up-titration, n (%)	4 (6.3)	8 (6.0)	7 (7.9)	1 (2.9)	0 (0.0)
Down-titration, n (%)	3 (4.8)	6 (4.5)	5 (5.6)	1 (2.9)	0 (0.0)
Dialysate calcium (mEq/L)					
<=2.0	1 (0.3)	2 (0.3)	2 (0.5)	0 (0.0)	0 (0.0)
>2.0 to <2.5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
>=2.5 to <3.0	146 (49.5)	306 (50.2)	209 (50.4)	77 (54.6)	20 (37.0)
>=3.0	137 (46.4)	284 (46.6)	194 (46.7)	58 (41.1)	32 (59.3)
Missing	11 (3.7)	18 (3.0)	10 (2.4)	6 (4.3)	2 (3.7)
Stable dose, n (%)	264 (93.0)	552 (93.7)	373 (92.6)	127 (94.8)	52 (100.0)
Up-titration, n (%)	8 (2.8)	13 (2.2)	11 (2.7)	2 (1.5)	0 (0.0)
Down-titration, n (%)	12 (4.2)	24 (4.1)	19 (4.7)	5 (3.7)	0 (0.0)

New users: no prescription in [DAY 31; DAY 60] of baseline but prescription in [DAY 61; DAY 90] of baseline
Continuing users: prescription in both [DAY 31; DAY 60] and [DAY 61; DAY 90] of baseline
Use = new users + continuing users
Stable dose: average daily dose between [DAY 31; DAY 60] = average daily dose between [DAY 61; DAY 90] of baseline
Up titration: average daily dose between [DAY 31; DAY 60] < average daily dose between [DAY 61; DAY 90] of baseline
Down titration: average daily dose between [DAY 31; DAY 60] > average daily dose between [DAY 61; DAY 90] of baseline

Table 4. Management of hypocalcemia within 30 days following first hypocalcemia event

	Within 30 days following hypocalcemia event											
				Ca at time of first hypocalcaemia								
	Overall			Ca >=2.00 - <2.10 mmol/L			Ca >=1.87 - <2.00 mmol/L			Ca <1.87 mmol/L		
Management of hypocalcemia following first hypocalcemia event	**No. at risk**	**n**	**%**	**No. at risk**	**n**	**%**	**No. at risk**	**n**	**%**	**No. at risk**	**n**	**%**
Cinacalcet												
Increased cinacalcet dose	610	59	9.7	415	45	10.8	141	13	9.2	54	1	1.9
Stable cinacalcet dose	610	479	78.5	415	327	78.8	141	107	75.9	54	45	83.3
Discontinued	610	9	1.5	415	8	1.9	141	0	0	54	1	1.9
Reduced cinacalcet dose	610	62	10.2	415	34	8.2	141	21	14.9	54	7	13
Discontinued or dose-reduced cinacalcet	610	71	11.6	415	42	10.1	141	21	14.9	54	8	14.8
Calcitriol/Alfacalcidol												
Initiated	486	21	4.3	326	11	3.4	115	6	5.2	45	4	8.9
Up-titrated	124	17	13.7	89	13	14.6	26	3	11.5	9	1	11.1
Initiated or up-titrated	610	38	6.2	415	24	5.8	141	9	6.4	54	5	9.3
Stable	124	91	73.4	89	66	74.2	26	18	69.2	9	7	77.8
Down-titrated	124	11	8.9	89	7	7.9	26	3	11.5	9	1	11.1
Discontinued	124	5	4	89	3	3.4	26	2	7.7	9	0	0
Discontinued or down-titrated	610	54	8.9	415	34	8.2	141	14	9.9	54	6	11.1
Paricalcitol												
Initiated	394	39	9.9	258	25	9.7	96	13	13.5	40	1	2.5
Up-titrated	216	38	17.6	157	27	17.2	45	8	17.8	14	3	21.4
Initiated or up-titrated	610	77	12.6	415	52	12.5	141	21	14.9	54	4	7.4
Stable	216	140	64.8	157	101	64.3	45	29	64.4	14	10	71.4
Down-titrated	216	22	10.2	157	17	10.8	45	4	8.9	14	1	7.1
Discontinued	216	16	7.4	157	12	7.6	45	4	8.9	14	0	0
Discontinued or down-titrated	610	115	18.9	415	81	19.5	141	29	20.6	54	5	9.3
Calcium-based phosphate binder												
Initiated	459	24	5.2	311	11	3.5	107	11	10.3	41	2	4.9
Up-titrated	151	14	9.3	104	7	6.7	34	5	14.7	13	2	15.4

Initiated or up-titrated	610	38	6.2	415	18	4.3	141	16	11.3	54	4	7.4
Stable	151	122	80.8	104	88	84.6	34	24	70.6	13	10	76.9
Down-titrated	151	8	5.3	104	4	3.8	34	3	8.8	13	1	7.7
Discontinued	151	7	4.6	104	5	4.8	34	2	5.9	13	0	0
Discontinued or down-titrated	610	53	8.7	415	27	6.5	141	21	14.9	54	5	9.3
Dialysate calcium												
Increased dialysate calcium	610	69	11.3	415	40	9.6	141	20	14.2	54	9	16.7
Stable dialysate calcium	610	510	83.6	415	353	85.1	141	114	80.9	54	43	79.6
Decreased dialysate calcium	610	10	1.6	415	9	2.2	141	1	0.7	54	0	0
Any responses[1]												
No treatment intervention	610	373	61.1	415	270	65.1	141	73	51.8	54	30	55.6
Any treatment intervention	610	237	38.9	415	145	34.9	141	68	48.2	54	24	44.4
Any responses[2]												
No treatment intervention	610	295	48.4	415	212	51.1	141	57	40.4	54	26	48.1
Any treatment intervention	610	315	51.6	415	203	48.9	141	84	59.6	54	28	51.9

[1]Any treatment = for Cinacalcet, discontinued or reduced; for Dialysate Calcium: increased calcium; for other drugs: initiated or up-titrated

[2]Any treatment = any of the changes listed in table