

**Supplementary Table S1.** Statistical analysis of pharmacokinetic parameters for 25(OH)D3 following repeated oral doses of cholecalciferol.

Time	25(OH)D3 (ng/ml)	ALL subjects (n=73)	Group A (n=24)	Group B (n=25)	Group C (n=24)	ANOVA p-value
V2 - Baseline	N	73	24	25	24	0.319
	Mean (SD)	13.5 (3.7)	14.4 (3.9)	12.8 (3)	13.4 (4.2)	
	Median (IQR)	13.8 (11.5-16)	14.7 (12.4-16.6)	12.6 (10.7-15.1)	13.4 (10-16.8)	
	Min-Max	5-21.9	7-21.9	5-18.4	5.9-19.8	
V3 – Day 7	N	73	24	25	24	<0.001
	Mean (SD)	23.3 (4.4)	23.5 (3.6)	20.9 (3)	25.7 (5.2)	
	Median (IQR)	22.7 (20.2-26.2)	22.9 (20.6-26.5)	20.6 (19.2-22.8)	25.9 (22.2-28.1)	
	Min-Max	14.2-35.6	14.2-29.6	15.3-26.4	14.7-35.6	
V4 – Day 14	N	73	24	25	24	<0.001
	Mean (SD)	28.2 (5.4)	32.5 (5)	26.5 (3.4)	25.6 (4.9)	
	Median (IQR)	28.4 (25.1-31)	32.2 (29.8-36.6)	26.6 (25.1-29.3)	24.8 (22.5-28.7)	
	Min-Max	17.2-40.4	20.5-40.4	18.9-31.8	17.2-34.7	
V5 – Day 21	N	73	24	25	24	<0.001
	Mean (SD)	38 (9.2)	44.2 (10.9)	34.1 (5.3)	35.8 (7.6)	
	Median (IQR)	36.5 (31.7-42.4)	42.6 (36-51.6)	34.2 (30.7-37.5)	36.5 (30.4-40.1)	
	Min-Max	18.8-70	21-70	22.7-45.6	18.8-49.2	
V6 – Day 28	N	73	24	25	24	<0.001
	Mean (SD)	43.6 (11.1)	55.2 (10.2)	38.9 (4.2)	36.9 (7.2)	
	Median (IQR)	41.2 (36.1-48.8)	55.6 (47.6-62)	39.2 (36.4-41.2)	36 (32.1-41.3)	
	Min-Max	25.9-85.2	40.4-85.2	29.6-48.8	25.9-59.2	
V7 – Day 35	N	73	24	25	24	<0.001
	Mean (SD)	49.9 (12.9)	62.6 (13)	43.6 (5.5)	43.8 (8.3)	
	Median (IQR)	46.8 (40-56.8)	63.2 (54.7-71.8)	43.6 (39.4-47.2)	43.8 (39.4-47.8)	
	Min-Max	26.5-84	33.8-84	36.3-54.8	26.5-57.6	
V8 – Day 42	N	73	24	25	24	<0.001
	Mean (SD)	54.6 (15.2)	71 (13.4)	49.4 (5.4)	43.5 (8.5)	
	Median (IQR)	51.6 (44-62)	68.4 (62.5-80.1)	49.2 (46-52.4)	43 (36.6-49)	
	Min-Max	29.4-100.4	47.2-100.4	39-60	29.4-62	
V9 – Day 49	N	73	24	25	24	<0.001
	Mean (SD)	56.3 (15)	72.4 (12.9)	51.1 (6.2)	45.7 (9)	
	Median (IQR)	51.6 (46.8-65.2)	70.8 (61.9-79.8)	50 (47.2-53.2)	45.6 (40-51.6)	
	Min-Max	28-97.6	49.6-97.6	42-65.2	28-65.6	
V10 – Day 56	N	73	24	25	24	<0.001
	Mean (SD)	59.6 (17.9)	79.1 (16.2)	53.5 (7.2)	46.4 (8.2)	
	Median (IQR)	55.2 (47.2-68.4)	78.6 (67.8-92.3)	52.8 (48.4-60)	47 (42.9-52.3)	
	Min-Max	31-113.6	49.2-113.6	40.4-68.4	31-59.6	
V11 – Day 63	N	73	24	25	24	<0.001
	Mean (SD)	57.7 (13.3)	70.8 (11.5)	52.8 (7)	49.8 (10.1)	
	Median (IQR)	54.4 (49.2-66.8)	71.6 (61.7-79.6)	51.6 (49.2-56.4)	49.2 (45.1-55.6)	
	Min-Max	32.5-90.4	52-90.4	40.8-72.8	32.5-71.2	
V12 – Day 77	N	73	24	25	24	0.039
	Mean (SD)	56.5 (10.8)	60.8 (11.6)	55.5 (7.8)	53.1 (11.6)	
	Median (IQR)	56 (48.8-63.2)	60.8 (53.3-70.2)	55.2 (48.8-60.8)	55 (43-60.2)	
	Min-Max	35.7-79.6	39.9-79.6	43.2-71.2	35.7-77.2	
V13 – Day 84	N	72	24	24	24	0.014
	Mean (SD)	55.1 (10.2)	56.9 (10.7)	58.2 (9.2)	50.3 (9.3)	
	Median (IQR)	53.8 (48.7-62.4)	54.8 (51.8-62.1)	57.2 (50.8-66)	49.6 (43.3-57.4)	
	Min-Max	33.2-80	40-80	43.6-74.8	33.2-66.4	
V14 – Day 85	N	67	24	21	22	0.012
	Mean (SD)	55.3 (10.5)	57.3 (11.5)	58.6 (8.2)	49.9 (9.6)	

	Median (IQR) Min-Max	56.8 (48.6-61.4) 32.2-77.6	57.2 (52.1-62.6) 32.2-77.6	60 (53.2-64.8) 42.4-76.8	49.2 (44.7-58.9) 33.7-64	
V15 – Day 87	N Mean (SD) Median (IQR) Min-Max	69 52.1 (10.1) 53.2 (46-58) 27.4-78.8	24 53.6 (11.5) 52.6 (47.6-57.8) 27.4-78.8	23 55.4 (6.6) 56 (52.8-59.4) 42.4-68.4	22 47 (10) 46.2 (40.9-53.2) 29-70	0.012
V16 - Day 89	N Mean (SD) Median (IQR) Min-Max	69 49.7 (9.6) 49.6 (41.6-56.4) 30.6-69.6	24 49.9 (8.7) 50.6 (43.4-55.4) 34.7-68.4	23 54.1 (9.5) 53.2 (49.6-60) 30.6-69.6	22 45 (8.9) 45.2 (37.4-51) 33.8-63.2	0.006
V17 - Day 96	N Mean (SD) Median (IQR) Min-Max	69 49.7 (11.2) 48.8 (41.2-55.2) 30.8-89.5	24 49.2 (9.7) 50.8 (41.2-55.6) 30.8-70	23 53 (10) 50.8 (47.6-55.2) 37.4-76.8	22 46.9 (13.2) 44.2 (39.4-49.4) 32.2-89.5	0.184
V18* Day 103	N Mean (SD) Median (IQR) Min-Max	69 41.1 (9.4) 40.4 (34.3-47.2) 25.6-68	24 41.1 (8.1) 41 (35.3-46.3) 25.6-58.8	23 44.3 (10.5) 40.8 (36.2-51.6) 27-68	22 37.8 (8.8) 35.9 (30.7-40.8) 25.6-60.4	0.065
V19* - Day 112	N Mean (SD) Median (IQR) Min-Max	69 43.5 (8.1) 42.4 (37.5-49.6) 27.6-64.4	24 44.4 (9.1) 42.6 (37.5-50.3) 31.6-64.4	23 45.3 (7.5) 44.4 (38.8-49.6) 34.4-61.6	22 40.8 (7.1) 39.4 (36-43.3) 27.6-56	0.15

**Supplementary Table S2.** Subjects with 25(OH)D levels  $\geq 20$  ng/mL and  $\geq 30$  ng/mL on Day 7, 14, 21, 28, 35, 42, 49, 56, 63, 77, 84, 85, 87, 89, 96, 103, 112.

Levels	ALL subjects (n=71)	Group A (n=24)	Group B (n=23)	Group C (n=24)
<b><math>\geq 20</math>ng/mL</b>				
Number of subjects with 25-OH-D <20ng/ml at baseline	69	22	23	24
Number of subjects with 25-OH-D $\geq 20$ ng/ml on Day 7	55/69 (79.7%)	19/22 (86.3%)	15/23 (65.2%)	21/24 (87.5%)
Number of subjects with 25-OH-D $\geq 20$ ng/ml on Day 14	65/69 (94.2%)	22/22 (100%)	22/23 (95.6%)	21/24 (87.5%)
Number of subjects with 25-OH-D $\geq 20$ ng/ml on Day 21	68/69 (98.6%)	22/22 (100%)	23/23 (100%)	23/24 (95.8%)
Number of subjects with 25-OH-D $\geq 20$ ng/ml on Day 28	69/69 (100%)	22/22 (100%)	23/23 (100%)	24/24 (100%)
Number of subjects with 25-OH-D $\geq 20$ ng/ml on Day 35	69/69 (100%)	22/22 (100%)	23/23 (100%)	24/24 (100%)
Number of subjects with 25-OH-D $\geq 20$ ng/ml on Day 42	69/69 (100%)	22/22 (100%)	23/23 (100%)	24/24 (100%)
Number of subjects with 25-OH-D $\geq 20$ ng/ml on Day 49	69/69 (100%)	22/22 (100%)	23/23 (100%)	24/24 (100%)
Number of subjects with 25-OH-D $\geq 20$ ng/ml on Day 56	69/69 (100%)	22/22 (100%)	23/23 (100%)	24/24 (100%)
Number of subjects with 25-OH-D $\geq 20$ ng/ml on Day 63	69/69 (100%)	22/22 (100%)	23/23 (100%)	24/24 (100%)
Number of subjects with 25-OH-D $\geq 20$ ng/ml on Day 77	69/69 (100%)	22/22 (100%)	23/23 (100%)	24/24 (100%)
Number of subjects with 25-OH-D $\geq 20$ ng/ml on Day 84	69/69 (100%)	22/22 (100%)	23/23 (100%)	24/24 (100%)
Number of subjects with 25-OH-D $\geq 20$ ng/ml on Day 85*	65/65 (100%)*	22/22 (100%)*	21/21 (100%)*	22/22 (100%)*
Number of subjects with 25-OH-D $\geq 20$ ng/ml on Day 87*	65/65 (100%)*	22/22 (100%)*	21/21 (100%)*	22/22 (100%)*
Number of subjects with 25-OH-D $\geq 20$ ng/ml on Day 89*	65/65 (100%)*	22/22 (100%)*	21/21 (100%)*	22/22 (100%)*
Number of subjects with 25-OH-D $\geq 20$ ng/ml on Day 96*	65/65 (100%)*	22/22 (100%)*	21/21 (100%)*	22/22 (100%)*
Number of subjects with 25-OH-D $\geq 20$ ng/ml on Day 103*	65/65 (100%)*	22/22 (100%)*	21/21 (100%)*	22/22 (100%)*
Number of subjects with 25-OH-D $\geq 20$ ng/ml on Day 112*	65/65 (100%)*	22/22 (100%)*	21/21 (100%)*	22/22 (100%)*
<b><math>\geq 30</math>ng/mL</b>				
Number of subjects with 25-OH-D <30ng/ml at baseline	71	24	23	24
Number of subjects with 25-OH-D $\geq 30$ ng/ml on Day 7	3/71 (4.2%)	0/24 (0%)	0/23 (0%)	3/24 (12.5%)
Number of subjects with 25-OH-D $\geq 30$ ng/ml on Day 14	26/71 (36.6%)	17/24 (70.8%)	4/23 (17.4%)	5/24 (20.8%)
Number of subjects with 25-OH-D $\geq 30$ ng/ml on Day 21	59/71 (83.1%)	22/24 (91.7%)	18/23 (78.3%)	19/24 (79.2%)
Number of subjects with 25-OH-D $\geq 30$ ng/ml on Day 28	66/71 (93%)	24/24 (100%)	22/23 (95.7%)	20/24 (83.3%)
Number of subjects with 25-OH-D $\geq 30$ ng/ml on Day 35	70/71 (98.6%)	24/24 (100%)	23/23 (100%)	23/24 (95.8%)
Number of subjects with 25-OH-D $\geq 30$ ng/ml on Day 42	70/71 (98.6%)	24/24 (100%)	23/23 (100%)	23/24 (95.8%)
Number of subjects with 25-OH-D $\geq 30$ ng/ml on Day 49	70/71 (98.6%)	24/24 (100%)	23/23 (100%)	23/24 (95.8%)
Number of subjects with 25-OH-D $\geq 30$ ng/ml on Day 56	71/71 (100%)	24/24 (100%)	23/23 (100%)	24/24 (100%)
Number of subjects with 25-OH-D $\geq 30$ ng/ml on Day 63	71/71 (100%)	24/24 (100%)	23/23 (100%)	24/24 (100%)
Number of subjects with 25-OH-D $\geq 30$ ng/ml on Day 77	71/71 (100%)	24/24 (100%)	23/23 (100%)	24/24 (100%)
Number of subjects with 25-OH-D $\geq 30$ ng/ml on Day 84	71/71 (100%)	24/24 (100%)	23/23 (100%)	24/24 (100%)
Number of subjects with 25-OH-D $\geq 30$ ng/ml on Day 85**	67/67 (100%)**	24/24 (100%)**	21/21 (100%)**	22/22 (100%)**
Number of subjects with 25-OH-D $\geq 30$ ng/ml on Day 87**	65/67 (97%)**	23/24 (95.8%)**	21/21 (100%)**	21/22 (95.5%)**
Number of subjects with 25-OH-D $\geq 30$ ng/ml on Day 89**	67/67 (100%)**	24/24 (100%)**	21/21 (100%)**	22/22 (100%)**
Number of subjects with 25-OH-D $\geq 30$ ng/ml on Day 96**	67/67 (100%)**	24/24 (100%)**	21/21 (100%)**	22/22 (100%)**
Number of subjects with 25-OH-D $\geq 30$ ng/ml on Day 103**	63/67 (94%)**	23/24 (95.8%)**	20/21 (95.2%)**	20/22 (90.9%)**
Number of subjects with 25-OH-D $\geq 30$ ng/ml on Day 112**	66/67 (98.5%)**	24/24 (100%)**	21/21 (100%)**	21/22 (95.5%)**

\* 4 subjects who took a dose on Day 84 (not per-protocol) are excluded from statistics of V14-V19. Percentages computed on 65 (69-4)

\*\* 4 subjects who took a dose on Day 84 (not per-protocol) are excluded from statistics of V14-V19. Percentages computed on 67 (71-4)

**Supplementary Table S3.** Pharmacodynamic parameters over time

Time		ALL subjects (n=73)	Group A (n=24)	Group B (n=25)	Group C (n=24)	ANOVA p-value
<b>Calcium</b>						
V2	N	73	24	25	24	0.372
	Mean (SD)	2.3 (0.1)	2.3 (0.1)	2.3 (0.1)	2.3 (0.1)	
	Median (IQR)	2.3 (2.2-2.4)	2.3 (2.3-2.4)	2.3 (2.2-2.3)	2.3 (2.2-2.4)	
	Min-Max	2.2-2.5	2.2-2.5	2.2-2.4	2.2-2.5	
V6	N	73	24	25	24	0.285
	Mean (SD)	2.3 (0.1)	2.3 (0.1)	2.3 (0.1)	2.3 (0.1)	
	Median (IQR)	2.3 (2.3-2.4)	2.3 (2.3-2.3)	2.3 (2.3-2.4)	2.3 (2.3-2.4)	
	Min-Max	2.1-2.5	2.1-2.5	2.2-2.4	2.2-2.5	
V10	N	73	24	25	24	0.956
	Mean (SD)	2.3 (0.1)	2.3 (0.1)	2.3 (0.1)	2.3 (0.1)	
	Median (IQR)	2.3 (2.3-2.4)	2.4 (2.3-2.4)	2.3 (2.3-2.4)	2.3 (2.3-2.4)	
	Min-Max	2.2-2.5	2.2-2.5	2.2-2.5	2.2-2.5	
V13	N	72	24	24	24	0.958
	Mean (SD)	2.3 (0.1)	2.3 (0.1)	2.3 (0.1)	2.3 (0.1)	
	Median (IQR)	2.3 (2.3-2.4)	2.3 (2.3-2.4)	2.3 (2.3-2.4)	2.3 (2.3-2.4)	
	Min-Max	2.1-2.5	2.2-2.4	2.1-2.5	2.2-2.4	
V19*	N	68	23	23	22	0.396
	Mean (SD)	2.3 (0.1)	2.3 (0.1)	2.3 (0.1)	2.3 (0.1)	
	Median (IQR)	2.3 (2.3-2.4)	2.3 (2.3-2.3)	2.3 (2.2-2.3)	2.4 (2.3-2.4)	
	Min-Max	2.2-2.5	2.2-2.5	2.2-2.5	2.2-2.5	
<b>Ionized calcium</b>						
V2	N	73	24	25	24	0.208
	Mean (SD)	1.2 (0)	1.2 (0)	1.2 (0)	1.2 (0)	
	Median (IQR)	1.2 (1.2-1.2)	1.2 (1.2-1.3)	1.2 (1.2-1.2)	1.2 (1.2-1.2)	
	Min-Max	1.2-1.3	1.2-1.3	1.2-1.3	1.2-1.3	
V6	N	72	24	24	24	0.636
	Mean (SD)	1.2 (0)	1.2 (0)	1.2 (0)	1.2 (0)	
	Median (IQR)	1.2 (1.2-1.2)	1.2 (1.2-1.2)	1.2 (1.2-1.2)	1.2 (1.2-1.2)	
	Min-Max	1-1.3	1-1.3	1.2-1.3	1.2-1.3	
V10	N	73	24	25	24	0.486
	Mean (SD)	1.2 (0)	1.2 (0)	1.2 (0)	1.2 (0)	
	Median (IQR)	1.2 (1.2-1.3)	1.2 (1.2-1.3)	1.2 (1.2-1.3)	1.2 (1.2-1.3)	
	Min-Max	1.2-1.3	1.2-1.3	1.2-1.3	1.2-1.3	
V13	N	72	24	24	24	0.674
	Mean (SD)	1.2 (0)	1.2 (0)	1.2 (0)	1.2 (0)	
	Median (IQR)	1.2 (1.2-1.2)	1.2 (1.2-1.2)	1.2 (1.2-1.2)	1.2 (1.2-1.2)	
	Min-Max	1.2-1.3	1.2-1.3	1.2-1.3	1.2-1.3	
V19*	N	69	24	23	22	0.373
	Mean (SD)	1.2 (0)	1.2 (0)	1.2 (0)	1.2 (0)	
	Median (IQR)	1.2 (1.2-1.2)	1.2 (1.2-1.2)	1.2 (1.2-1.2)	1.2 (1.2-1.2)	
	Min-Max	1.1-1.3	1.2-1.3	1.2-1.3	1.1-1.3	
<b>Albumin</b>						
V2	N	73	24	25	24	0.323
	Mean (SD)	44.9 (2.6)	45.2 (2.8)	44.3 (2.8)	45.3 (2.2)	
	Median (IQR)	45.3 (43-46.8)	45.4 (43.3-47.4)	44.2 (42.2-45.8)	45.1 (43.4-47.3)	
	Min-Max	40.1-52.6	40.3-49.6	40.1-52.6	42.1-48.9	
V6	N	73	24	25	24	0.427
	Mean (SD)	45.1 (3)	45.4 (4)	44.5 (2.6)	45.5 (2.1)	
	Median (IQR)	45.1 (43-46.6)	45.7 (42.1-48.4)	44.3 (42.7-46.1)	45.3 (44.4-46.8)	
	Min-Max	36.7-52.1	36.7-52.1	38.7-52	42.2-50.1	
V10	N	73	24	25	24	0.354
	Mean (SD)	45.3 (2.7)	46 (2.4)	45.1 (2.9)	44.9 (2.7)	
	Median (IQR)	45.1 (43.4-46.6)	46 (43.7-48)	44.7 (42.9-46.3)	44.7 (43.1-45.3)	
	Min-Max	40.5-53.7	41.7-49.9	40.6-53.7	40.5-51.9	
V13	N	72	24	24	24	0.813
	Mean (SD)	44.7 (3.1)	45 (3.1)	44.4 (3.6)	44.8 (2.5)	
	Median (IQR)	44.8 (42.6-47.2)	45 (42.6-47.5)	44.9 (42.5-46)	44 (42.6-47.1)	
	Min-Max	34.5-52.1	38.8-50.2	34.5-52.1	41.2-48.7	

V19*	N	69	24	23	22	
	Mean (SD)	44.4 (2.6)	44.3 (2.3)	44.3 (3.4)	44.6 (1.9)	0.909
	Median (IQR)	44.7 (42.7-45.5)	44.9 (43.2-45.5)	43.7 (42.1-45.2)	44.7 (43.1-45.5)	
	Min-Max	39-52.6	39.2-48.7	39-52.6	41.6-49.7	
<b>Phosphate</b>						
V2	N	73	24	25	24	
	Mean (SD)	1.1 (0.2)	1.1 (0.2)	1.1 (0.1)	1.1 (0.2)	0.85
	Median (IQR)	1.1 (1-1.1)	1.1 (1-1.2)	1.1 (1-1.1)	1.1 (1-1.1)	
	Min-Max	0.6-1.6	0.7-1.5	0.9-1.2	0.6-1.6	
V6	N	73	24	25	24	
	Mean (SD)	1.1 (0.1)	1.1 (0.1)	1.1 (0.1)	1.1 (0.2)	0.503
	Median (IQR)	1.1 (1-1.2)	1.1 (1-1.2)	1.1 (1-1.2)	1.1 (1-1.2)	
	Min-Max	0.7-1.5	0.9-1.4	0.8-1.3	0.7-1.5	
V10	N	73	24	25	24	
	Mean (SD)	1.1 (0.2)	1.1 (0.2)	1.1 (0.1)	1.1 (0.2)	0.539
	Median (IQR)	1.1 (1-1.2)	1.1 (1-1.2)	1.1 (1-1.2)	1.1 (1-1.2)	
	Min-Max	0.7-1.5	0.8-1.5	0.8-1.4	0.7-1.5	
V13	N	72	24	24	24	
	Mean (SD)	1.1 (0.1)	1.1 (0.1)	1.1 (0.1)	1.1 (0.2)	0.267
	Median (IQR)	1.1 (1-1.2)	1.1 (1-1.2)	1.1 (1-1.1)	1.1 (1.1-1.2)	
	Min-Max	0.7-1.4	0.7-1.4	0.8-1.3	0.7-1.4	
V19*	N	69	24	23	22	
	Mean (SD)	1.1 (0.1)	1 (0.1)	1.1 (0.1)	1.1 (0.2)	0.839
	Median (IQR)	1.1 (1-1.1)	1 (1-1.1)	1 (1-1.1)	1.1 (1-1.1)	
	Min-Max	0.7-1.4	0.9-1.3	0.8-1.4	0.7-1.4	

**Supplementary Table S4.** Summary of adverse events during the study

	All AE (N)	All Subject N (%)	Group A AE (N)	Group A Subject N (%)	Group B AE (N)	Group B Subject N(%)	Group C AE (N)	Group C Subject N (%)
AEs	118	49 (65.3)	42	18 (72)	48	19 (76)	28	12 (48)
Mild AEs	86	38 (50.7)	33	15 (60)	34	13 (52)	19	10 (40)
Moderate AEs	32	25 (33.3)	9	8 (32)	14	10 (40)	9	7 (28)
Severe AEs	0	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)
SAEs	0	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)
IMP-related AEs (certain/probable/possible)	1	1 (1.3)	1	1 (4)	0	0 (0)	0	0 (0)
IMP-not related AEs (no reasonable causal relationship)*	117	49 (65.3)	41	18 (72)	48	19 (76)	28	12 (48)
AEs leading to withdrawal	1	1 (1.3)	1	1 (4)	0	0 (0)	0	0 (0)
<i>IMP: medicinal product (cholecalciferol)</i> <i>AE n: number of adverse events</i> <i>Subject n: number of subjects with AE</i> <i>* considering 'not related' and 'unlikely relationship'</i>								