

Supplementary Material Tables 1-3.

Supplementary Material Table 3. BMI median, interquartile range (IQR) and minimum and maximum values of the enrolled individuals at baseline.

Baseline		Total population (n=75)	Group A (n=25)	Group B (n=25)	Group C (n=25)
BMI (Kg/M ²)	Median [IQR] Min-max	22.82 21.22-24.6 19-28	23.01 21.49-26.02 19-28	22.78 21.84-24.79 20-27	21.67 20.37-24.37 19-28
Males	Median [IQR] Min-max	23.51 21.2-26.24 19-28	23.7 22.9-27.77 20-28	23.59 21.8-25.88 20-27	21.3 18.67-23.67 19-28
Females	Median [IQR] Min-max	22.35 20.95-24.29 19-27	22.59 20.10-23.82 19-27	22.43 21.78-24.38 20-27	22.04 20.59-25.17 19-27

Supplementary Material Table 2. Absolute levels of biochemical parameters at baseline and at the various time points.

Time		ALL subjects (n=73)	Group A (n=24)	Group B (n=25)	Group C (n=24)	ANOVA p-value
1,25-dihydroxyvitamin D (pg/mL)						
Baseline	N Mean (SD) Median (IQR)	73 44 (11.5) 43.7 (36.5-50.2) 16.8-77.1	24 42 (8.8) 43.5 (36.5-49.2) 24.4-58.4	25 47.2 (12.7) 45.4 (38.2-54.8) 28.2-77.1	24 42.8 (12.3) 40.5 (35.9-48.1) 16.8-65.5	0.234
Day 28	N Mean (SD) Median (IQR)	73 57 (15.4) 56.6 (44.3-63.3) 33.8-110	24 61.6 (16.9) 59.9 (48.5-71.7) 37.4-110	25 57.5 (14.6) 57.3 (45.9-61.7) 36.1-95.2	24 52 (13.5) 50 (42.4-60) 33.8-85.7	0.091
Day 56	N Mean (SD) Median (IQR)	73 56.8 (11.7) 54.5 (50.6-63.7) 23.7-97	24 59.2 (9.3) 57.2 (52.8-64.4) 44.4-81.4	25 56.6 (12.1) 53.8 (49-57.7) 42.6-97	24 54.5 (13.2) 53.5 (46.2-63.3) 23.7-79.7	0.387
Day 84	N Mean (SD) Median (IQR)	72 56.3 (13.1) 55.4 (47-65.2) 28.3-96.6	24 55.8 (13) 53.5 (46.8-64.7) 32.1-83.9	24 57.5 (14.4) 56.5 (47-64.9) 28.3-96.6	24 55.6 (12.1) 53.5 (46.7-66.7) 37.4-74.9	0.859
Day 112	N Mean (SD) Median (IQR)	69 48.2 (13.4) 46.2 (39-55) 24-104	24 47.2 (11.1) 47.7 (41.2-55.2) 24-63.4	23 51.6 (17.2) 48.4 (39.7-62.4) 25.2-104	22 45.7 (10.7) 44.1 (39.2-48.5) 25.3-70.3	0.314
24,25-dihydroxyvitamin D (ng/mL)						
Baseline	N Mean (SD)	73 93.9 (185.1)	24 98 (169)	25 105.6 (257.2)	24 77.7 (95.9)	0.866

	Median (IQR)	33.2 (16-90.1) 4.9-1308	31.5 (17.5-96.1) 9.9-817.6	29.4 (12.1-89.5) 4.9-1308	39.7 (17.2-84.7) 5.7-361.6	
Day 28	N Mean (SD) Median (IQR)	73 68.7 (152.8) 24.6 (16.8-53.5) 5.4-1077	24 77.4 (153.7) 24.4 (17.8-54.3) 8-760.7	25 80.4 (211.1) 24.6 (15.8-50.7) 5.5-1077	24 47.8 (48.4) 25 (18.9-63.8) 5.4-168.7	0.72
Day 56	N Mean (SD) Median (IQR)	73 50.5 (76.1) 28.5 (11.2-59.8) 0-574.2	24 72.4 (115.4) 37.8 (15.7-77.3) 6.6-574.2	25 43 (50.6) 23.1 (10.6-50) 0-184.4	24 36.6 (36.8) 22 (10.3-51) 7.5-133.5	0.22
Day 84	N Mean (SD) Median (IQR)	72 67.3 (170.3) 23.8 (13.8-56.2) 4-1399	24 58.3 (65.6) 32.2 (16.2-71.5) 9.7-268.1	24 98 (282.9) 21.8 (11.8-55) 5.4-1399	24 45.5 (60.3) 23.8 (13.1-52.5) 4-263	0.544
Day 112	N Mean (SD) Median (IQR)	69 53 (108.8) 20.9 (13.5-44.1) 3.6-814	24 45.6 (57.7) 27.1 (14.3-46.3) 3.6-266.7	23 66 (169) 19.1 (9.8-33.6) 3.8-814	22 47.5 (67) 20.8 (16.5-44.7) 5.4-305.2	0.786
PTH (pg/mL)						
Baseline	N Mean (SD) Median (IQR)	73 36.4 (14) 33.4 (25.9-43.1) 11.5-79.3	24 37.2 (15.4) 32.8 (25.6-43.1) 14.9-74.4	25 33.1 (10.5) 32.8 (25.5-40.9) 11.5-59.2	24 39.1 (15.7) 36 (27.2-48) 12.8-79.3	0.319
Day 28	N Mean (SD) Median (IQR)	73 31.7 (11.6) 30.8 (23.3-39.8) 8.3-67.8	24 31.6 (10.4) 33.1 (25.4-38.2) 13.5-56.8	25 30.5 (11.3) 29.4 (23.3-39.8) 8.3-51.5	24 32.9 (13.3) 31.8 (23.9-42.1) 13-67.8	0.772
Day 56	N Mean (SD) Median (IQR)	73 32.4 (14.5) 28.5 (23.6-37.9) 7.6-72.2	24 31.3 (13.6) 27.9 (23.5-34.6) 15.4-62.4	25 32.2 (13.1) 32.1 (25-39.5) 7.6-62.1	24 33.7 (17) 26.9 (22.5-38.7) 13.7-72.2	0.84
Day 84	N Mean (SD) Median (IQR)	72 31.6 (12.6) 30.1 (23.2-37.1) 7.2-78.6	24 32.6 (11.9) 28.4 (25.3-37.5) 14-60.9	24 28 (11.3) 27.5 (20.8-34.4) 7.2-56.9	24 34.1 (14.2) 31.3 (27.7-38.2) 13.3-78.6	0.221
Day 112*	N Mean (SD) Median (IQR)	69 34 (13) 31.1 (25.7-42.1) 9.2-73.1	24 34.9 (12.5) 29.9 (26.7-45.5) 18.4-63.2	23 32.3 (9.9) 32.5 (27-36.3) 10.2-50	22 34.8 (16.4) 30.4 (23.9-41.7) 9.2-73.1	0.753
Ionized calcium (mmol/L)						
Baseline	N Mean (SD) Median (IQR)	73 1.2 (0) 1.2 (1.2-1.2) 1.2-1.3	24 1.2 (0) 1.2 (1.2-1.3) 1.2-1.3	25 1.2 (0) 1.2 (1.2-1.2) 1.2-1.3	24 1.2 (0) 1.2 (1.2-1.2) 1.2-1.3	0.208
Day 28	N Mean (SD) Median	72 1.2 (0)	24 1.2 (0)	24 1.2 (0)	24 1.2 (0)	0.636

	(IQR)	1.2 (1.2-1.2) 1-1.3	1.2 (1.2-1.2) 1-1.3	1.2 (1.2-1.2) 1.2-1.3	1.2 (1.2-1.2) 1.2-1.3	
Day 56	N Mean (SD) Median (IQR)	73 1.2 (0) 1.2 (1.2-1.3) 1.2-1.3	24 1.2 (0) 1.2 (1.2-1.3) 1.2-1.3	25 1.2 (0) 1.2 (1.2-1.3) 1.2-1.3	24 1.2 (0) 1.2 (1.2-1.3) 1.2-1.3	0.486
Day 84	N Mean (SD) Median (IQR)	72 1.2 (0) 1.2 (1.2-1.2) 1.2-1.3	24 1.2 (0) 1.2 (1.2-1.2) 1.2-1.3	24 1.2 (0) 1.2 (1.2-1.2) 1.2-1.3	24 1.2 (0) 1.2 (1.2-1.2) 1.2-1.3	0.674
Day 112	N Mean (SD) Median (IQR)	69 1.2 (0) 1.2 (1.2-1.2) 1.1-1.3	24 1.2 (0) 1.2 (1.2-1.2) 1.2-1.3	23 1.2 (0) 1.2 (1.2-1.2) 1.2-1.3	22 1.2 (0) 1.2 (1.2-1.2) 1.1-1.3	0.373
FGF-23 (pmol/L)						
Baseline	N Mean (SD) Median (IQR)	73 1 (1.6) 0.5 (0.3-1) 0-10.8	24 0.5 (0.4) 0.4 (0.2-0.8) 0-1.6	25 1.3 (2.2) 0.6 (0.3-1.1) 0-10.8	24 1.1 (1.4) 0.6 (0.3-1.1) 0-5.4	0.192
Day 28	N Mean (SD) Median (IQR)	73 1.4 (2.8) 0.8 (0.4-1.4) 0-22.5	24 0.7 (0.6) 0.6 (0.4-0.8) 0-2.7	25 2.2 (4.4) 1.2 (0.4-1.7) 0-22.5	24 1.4 (1.8) 0.6 (0.4-1.5) 0-7.8	0.19
Day 56	N Mean (SD) Median (IQR)	73 1.3 (1.6) 0.7 (0.3-1.4) 0-9.5	24 0.8 (0.9) 0.6 (0.3-1) 0-3.9	25 1.7 (2.2) 0.8 (0.5-2) 0-9.5	24 1.2 (1.4) 0.7 (0.4-1.5) 0.2-6.7	0.154
Day 84	N Mean (SD) Median (IQR)	72 1.2 (1.4) 0.7 (0.3-1.3) 0-6.1	24 0.8 (0.9) 0.4 (0.3-1) 0-3.7	24 1.3 (1.4) 1 (0.2-1.6) 0-5.9	24 1.4 (1.6) 0.7 (0.5-1.3) 0-6.1	0.208
Day 112	N Mean (SD) Median (IQR)	69 1.3 (1.9) 0.8 (0.4-1.2) 0.1-12	24 0.7 (0.5) 0.6 (0.3-1) 0.1-2.1	23 1.7 (2.6) 1 (0.4-1.8) 0.2-12	22 1.6 (1.8) 0.8 (0.6-2) 0.1-7.8	0.155
CTX-I (ng/mL)						
Baseline	N Mean (SD) Median (IQR)	73 0.4 (0.2) 0.3 (0.2-0.5) 0.1-0.9	24 0.4 (0.2) 0.4 (0.3-0.5) 0.1-0.9	25 0.3 (0.2) 0.3 (0.2-0.4) 0.1-0.8	24 0.3 (0.1) 0.4 (0.3-0.4) 0.1-0.5	0.022
Day 28	N Mean (SD) Median (IQR)	73 0.4 (0.2) 0.4 (0.3-0.5) 0.1-1.1	24 0.4 (0.2) 0.4 (0.3-0.6) 0.1-1.1	25 0.3 (0.1) 0.3 (0.2-0.4) 0.1-0.7	24 0.4 (0.2) 0.4 (0.3-0.5) 0.1-0.7	0.07
Day 56	N Mean (SD) Median	73 0.3 (0.2) 0.3 (0.2-0.5) 0-0.7	24 0.4 (0.2) 0.4 (0.2-0.6) 0.1-0.7	25 0.3 (0.1) 0.2 (0.2-0.4) 0.1-0.6	24 0.3 (0.1) 0.3 (0.2-0.4) 0-0.5	0.042

	(IQR)					
Day 84	N Mean (SD) Median (IQR)	72 0.4 (0.2) 0.3 (0.2-0.5) 0-0.8	24 0.4 (0.2) 0.4 (0.3-0.5) 0.2-0.8	24 0.3 (0.2) 0.3 (0.2-0.4) 0.1-0.8	24 0.3 (0.2) 0.3 (0.2-0.5) 0-0.7	0.068
Day 112	N Mean (SD) Median (IQR)	69 0.3 (0.2) 0.3 (0.2-0.4) 0-0.8	24 0.4 (0.2) 0.4 (0.2-0.5) 0.1-0.8	23 0.3 (0.2) 0.3 (0.2-0.4) 0.1-0.6	22 0.3 (0.2) 0.3 (0.2-0.4) 0-0.6	0.09
P1NP (ng/mL)						
Baseline	N Mean (SD) Median (IQR)	73 62.6 (24.1) 58 (45.9-72.2) 22.7-149.8	24 75.9 (29) 68.2 (57.9-90.9) 22.7-149.8	25 53.8 (18.7) 50.5 (42.5-57.1) 28.6-128.1	24 58.6 (18.2) 58.3 (43.5-71.4) 32.9-88.9	0.003
Day 28	N Mean (SD) Median (IQR)	73 64.8 (25.4) 60.4 (49.6-70) 25.1-153.6	24 80.5 (33.7) 67.3 (57.7-102.9) 25.1-153.6	25 55.9 (15.5) 54.4 (47.9-61.3) 28.6-103.3	24 58.4 (15.4) 60.1 (46-68.7) 32.8-92.5	0.001
Day 56	N Mean (SD) Median (IQR)	73 61.8 (22.4) 56.4 (46.5-75.4) 23.5-145.9	24 71.5 (28) 61.9 (53.5-82.2) 23.5-145.9	25 54.2 (16.3) 49.8 (45.3-61.8) 32.6-104.6	24 60.1 (18.8) 56.5 (44.1-75.6) 29.5-99.2	0.021
Day 84	N Mean (SD) Median (IQR)	72 60.3 (25.7) 56.4 (41.9-70.7) 25.3-195.7	24 72.6 (34.2) 66.2 (53.1-87.3) 27.3-195.7	24 50.8 (18) 46.1 (37.8-63.1) 25.3-87.6	24 57.4 (16.7) 55.9 (42.3-67.3) 33.9-88.2	0.009
Day 112	N Mean (SD) Median (IQR)	69 57.3 (20.7) 55.9 (42-66.7) 23.6-109.5	24 67.2 (23.2) 61.8 (53.7-81.9) 23.6-107.4	23 50.4 (16.1) 48.4 (41-55.2) 27.8-100	22 53.8 (18.8) 51.7 (37.9-65.5) 29.5-109.5	0.012
BALP (ug/L)						
Baseline	N Mean (SD) Median (IQR)	73 15.6 (6.7) 13.9 (11.1-18.3) 5.8-40.7	24 18 (8.5) 16.4 (12.5-20.8) 7.3-40.7	25 13.8 (3.9) 12.8 (11.1-15.6) 7.5-24.7	24 15.2 (6.6) 14.2 (10.4-18.3) 5.8-33.5	0.08
Day 28	N Mean (SD) Median (IQR)	73 15.1 (5.9) 14.2 (11.2-17.4) 3.3-34.5	24 17.2 (6.2) 16.6 (12.6-20.8) 6.7-33.2	25 13.7 (4.1) 12.9 (10.8-15.7) 8.7-24.2	24 14.5 (6.7) 14 (10.3-16.5) 3.3-34.5	0.093
Day 56	N Mean (SD) Median (IQR)	73 14.8 (6.7) 13.6 (10.8-16.8) 5.6-44.6	24 17.1 (8.1) 15.3 (12.3-18.5) 6-44.6	25 13.1 (4) 12.7 (10.1-14.8) 6.3-20.7	24 14.5 (7) 13.4 (10.6-15.8) 5.6-33.8	0.105
Day 84	N Mean (SD) Median	72 14.5 (6.4) 13.2 (10.6-15.9) 5.7-37.6	24 17.2 (7.6) 15.3 (12.2-22) 5.7-37.6	24 12.3 (3.6) 11.3 (10.3-14.4) 7.3-21.1	24 14 (6.5) 13.3 (11-14.2) 6.2-36.5	0.027

	(IQR)					
Day 112	N Mean (SD) Median (IQR)	69 13.8 (6.2) 12.4 (10.1-16.8) 4.2-43	24 16.1 (8.1) 13.8 (10.3-19.5) 6-43	23 12.1 (3.5) 11.2 (9.4-13.9) 7-20.9	22 13.1 (5.4) 12.4 (10-15.5) 4.2-27.9	0.065
Dkk-1 (pmol/L)						
Baseline	N Mean (SD) Median (IQR)	73 18.6 (11.1) 15.7 (10.6-23.1) 2.2-56	24 16.7 (8.3) 17.3 (11.9-23.2) 2.2-32.6	25 17.7 (12.6) 13.7 (10.3-21) 4-50.3	24 21.2 (11.9) 18.6 (13.3-26.4) 6.1-56	0.339
Day 28	N Mean (SD) Median (IQR)	73 19.1 (11.2) 16 (10.7-23.6) 4-60.8	24 18 (8.6) 16 (12.2-23.4) 5.6-39.9	25 17.5 (11) 15.3 (9.7-20.6) 4-44.4	24 21.9 (13.3) 18.1 (12.5-27.7) 7-60.8	0.329
Day 56	N Mean (SD) Median (IQR)	73 22.7 (12.1) 21.1 (13.8-31.6) 5-64.5	24 21.3 (10.1) 21.6 (12.6-27.5) 5-37.5	25 21.5 (12.1) 16.6 (11.4-31.6) 5.6-45.5	24 25.4 (13.8) 22.4 (14.7-32.4) 8.7-64.5	0.421
Day 84	N Mean (SD) Median (IQR)	72 24.8 (14.2) 21.7 (12.7-34.5) 4.5-63.6	24 23.7 (13.1) 20.2 (13.7-31.8) 6-53	24 24.7 (14.3) 22.3 (11.9-35) 6.3-53.3	24 25.9 (15.5) 22.6 (14.3-35.4) 4.5-63.6	0.873
Day 112	N Mean (SD) Median (IQR)	69 23.9 (12.7) 21.6 (14.1-31.4) 5-54.5	24 21.8 (11.7) 21.4 (11.8-30.1) 5.3-45.4	23 23.3 (13.2) 21.6 (13-30.2) 5-51.9	22 26.7 (13.1) 22.1 (18.2-33.1) 9.9-54.5	0.419
Sclerostin (pmol/L)						
Baseline	N Mean (SD) Median (IQR)	73 25 (25.5) 18.9 (11.9-31.7) 4.1-173	24 20.5 (13.7) 16.8 (11.8-24.4) 4.1-66.2	25 28.2 (27) 19.5 (11.9-36.4) 5.8-139.1	24 26.1 (32.5) 19.2 (15.5-25.1) 5-173	0.559
Day 28	N Mean (SD) Median (IQR)	73 22.3 (20.6) 17.9 (11.6-25.7) 0-151.8	24 18.1 (13.1) 16.6 (9.1-22.9) 0-57.9	25 22.7 (15.9) 17.9 (13.8-28.6) 0-82.2	24 26 (29.3) 19.2 (14.7-25.5) 0-151.8	0.419
Day 56	N Mean (SD) Median (IQR)	73 25.2 (22) 20.5 (14.2-31.7) 0-150	24 20.1 (15.2) 19.7 (11.1-25.9) 0-63.3	25 27.3 (20.6) 24.9 (15-33.9) 6.2-106.8	24 28.1 (28.2) 20 (15.9-32.7) 7.8-150	0.382
Day 84	N Mean (SD) Median (IQR)	72 24 (17.9) 19 (13.3-28.3) 0-111.1	24 20.9 (13.2) 18.4 (11.2-26.7) 4.5-52.5	24 27 (18.7) 20.9 (14.9-34.8) 5.2-89.9	24 24.1 (21.1) 19.7 (13.2-25.5) 0-111.1	0.504
Day 112	N Mean (SD) Median	69 25.6 (16.8) 20.3 (14-33.4) 6.2-98	24 24.1 (13.9) 19 (16.4-32.5) 7.6-57.7	23 28 (20.7) 19.7 (13.8-33.9) 6.2-98	22 24.5 (15.6) 22 (13.6-28.7) 8.1-76	0.691

	(IQR)					
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Supplementary Material Table 3. Percentage change of the tested biochemical parameters with respect to baseline at the various time points.

Time		ALL subjects (n=73)	Group A (n=24)	Group B (n=25)	Group C (n=24)		ANOVA Results
1,25-dihydroxyvitamin D							
Day 28 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	73 34 (35) 25.8;42.2 <0.001 33 (11.4;49.8)	24 50 (38.3) 33.8;66.1 <0.001 40.7 (25.4;76.1)	25 25.8 (29.5) 13.6;38 <0.001 28.6 (6.4;44.3)	24 26.6 (32.7) 12.7;40.4 0.001 19.5 (8.9;41)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.022 0.014 0.019 0.941 0.043 0.043 0.941
Day 56 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	73 34.1 (30.8) 26.9;41.2 <0.001 35.1 (11.6;49)	24 45.3 (29.1) 33;57.6 <0.001 41.5 (26.3;51.4)	25 25.2 (29.8) 12.9;37.5 <0.001 23.1 (0;42.1)	24 32.1 (31.2) 18.9;45.3 <0.001 26 (10.5;51)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.067 0.022 0.133 0.425 0.067 0.267 0.425
Day 84 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	72 31.5 (29.5) 24.6;38.4 <0.001 30.9 (7.4;44.2)	24 34.2 (22.6) 24.7;43.8 <0.001 32.7 (18.6;42.9)	24 23.7 (29) 11.4;35.9 0.001 22 (2.8;38.7)	24 36.6 (35) 21.8;51.4 <0.001 32.3 (13.3;63.6)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.273 0.218 0.776 0.131 0.435 0.776 0.392
Day 112 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	69 13.1 (26.2) 6.8;19.4 <0.001 10 (-6.4;27.9)	24 14.4 (26.4) 3.2;25.5 0.014 11.2 (3.2;22)	23 11.1 (28.9) -1.5;23.6 0.08 3.3 (-8.8;31.6)	22 13.9 (24.2) 3.2;24.7 0.013 8.1 (-6.1;29.5)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.9 0.672 0.959 0.717 1 1 1
24,25-dihydroxyvitamin D							
Day 28 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	73 11.6 (134.8) -19.9;43.1 0.464 -17.7 (-49.5;27.2)	24 -4.7 (49.5) -25.6;16.2 0.645 -11.3 (-33.7;27.7)	25 46.6 (213.1) -41.4;134.5 0.285 -9.6 (-50.8;65.7) -	24 -8.5 (70.8) -38.4;21.4 0.562 -25.1 (-49.9;15.1)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.281 0.186 0.922 0.156 0.467 0.922 0.467

Day 56 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	73 -0.8 (83) -20.2;18.6 0.935 -25.3 (-57.7;29.5)	24 13.9 (93) -25.3;53.2 0.47 -23.6 (-46.3;41.5) -	25 9.2 (93.7) -29.5;47.8 0.629 -13.2 (-53.4;47.8)	24 -25.9 (52.5) -48.1;-3.7 0.024 -37.4 (-61.8;4.1)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.192 0.839 0.098 0.14 0.839 0.293 0.293
Day 84 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	72 1.4 (91) -20;22.8 0.898 -17.6 (-63.8;29.7)	24 15.6 (116) -33.4;64.6 0.517 2.7 (-62.3;29.7)	24 -0.1 (68.1) -28.9;28.7 0.995 -11.3 (-52.8;40.5)	24 -11.4 (84.1) -46.9;24.1 0.515 -32.4 (-66.1;18.3)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.595 0.555 0.312 0.671 1 0.935 1
Day 112 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	69 -1.2 (112.1) -28.1;25.7 0.929 -29.3 (-61.9;21.1)	24 -9.9 (73.9) -41.1;21.3 0.519 -27.3 (-69.7;17.9)	23 26.1 (172.1) -48.4;100.5 0.475 -42.6 (-57.9;54.8)	22 -20.2 (49.2) -42.1;1.6 0.067 -25.1 (-60.5;11.8)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.348 0.275 0.755 0.17 0.551 0.755 0.511
PTH							
Day 28 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	73 -7.7 (35.2) -15.9;0.5 0.065 -14.4 (-34.2;9.4)	24 -6.6 (40.8) -23.8;10.7 0.438 -13.7 (-35.3;11.5)	25 -5 (33.9) -19;9.1 0.473 -12.3 (-27.2;15.9)	24 -11.8 (31.2) -24.9;1.4 0.078 -20 (-32.4;0)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.785 0.873 0.615 0.505 1 1 1
Day 56 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	73 -7.1 (35.9) -15.5;1.3 0.097 -15.2 (-27.6;6.6)	24 -9.4 (41.5) -26.9;8.1 0.279 -20.4 (-29.1;3.2)	25 -0.1 (37.8) -15.7;15.6 0.994 -7.9 (-21.4;7.6)	24 -12 (27.2) -23.5;-0.6 0.04 -15.5 (-34.3;3.3)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.476 0.368 0.799 0.249 0.746 0.799 0.746
Day 84 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	72 -8.3 (31.2) -15.6;-1 0.026 -10.5 (-38;14.9)	24 -6.5 (28.5) -18.5;5.5 0.275 -8.6 (-25.4;12.2)	24 -11.9 (31.6) -25.2;1.4 0.078 -10.7 (-38;8)	24 -6.6 (34.2) -21;7.9 0.356 -10.5 (-40.1;17.2)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.793 0.554 0.994 0.559 1 1 1
Day 112 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	69 1.2 (38.8) -8.2;10.5 0.804 -6.4 (-23.7;15.5)	24 3.9 (44.5) -14.9;22.7 0.673 -3 (-27.3;21.8)	23 0.9 (25.3) -10.1;11.8 0.87 -11.2 (-21.6;17.1)	22 -1.5 (44.9) -21.4;18.4 0.877 -6.6 (-23.2;11.3)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.897 0.794 0.644 0.84 1 1 1
Ionized calcium							
Day 28 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	72 -0.7 (3.2) -1.5;0 0.048 -0.8 (-2.4;0.8)	24 -1.7 (3.8) -3.3;-0.1 0.036 -1.2 (-3.2;0)	24 -0.2 (3.2) -1.5;1.2 0.793 -0.4 (-2.6;1.1)	24 -0.4 (2.3) -1.3;0.6 0.433 -0.8 (-1.7;0.8)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.189 0.094 0.144 0.825 0.281 0.287 0.825

Day 56 percentage change with respect to Baseline	N	73	24	25	24	P anova	0.71
	Mean (SD)	0.8 (2.8)	0.4 (2.9)	0.8 (2.8)	1.1 (2.8)	P AvsB	0.573
	95%CI	0.1;1.4	-0.8;1.6	-0.3;2	-0.1;2.2	P AvsC	0.421
	p-value#	0.022	0.51	0.14	0.08	P BvsC	0.802
	Median (IQR)	0.9 (-1.6;2.5)	0.4 (-1.2;2.4)	0.8 (-0.8;2.4)	2.4 (-1.6;3.3)	P AvsB (Holm)	1
			-5.6;5.9	-4;8.6	-3.2;6	P AvsC (Holm)	1
						P BvsC (Holm)	1
Day 84 percentage change with respect to Baseline	N	72	24	24	24	P anova	0.359
	Mean (SD)	-0.1 (2.6)	-0.4 (2.1)	0.5 (2.7)	-0.4 (2.9)	P AvsB	0.22
	95%CI	-0.7;0.5	-1.3;0.5	-0.6;1.7	-1.7;0.8	P AvsC	0.983
	p-value#	0.717	0.335	0.363	0.479	P BvsC	0.212
	Median (IQR)	-0.4 (-1.6;1.7)	-0.8 (-1.6;1.6)	0 (-0.8;1.9)	-0.8 (-1.8;0.4)	P AvsB (Holm)	0.635
						P AvsC (Holm)	0.983
						P BvsC (Holm)	0.635
Day 112 percentage change with respect to Baseline	N	69	24	23	22	P anova	0.775
	Mean (SD)	-0.9 (2.5)	-1.2 (2.5)	-0.7 (2.3)	-0.7 (2.7)	P AvsB	0.533
	95%CI	-1.5;-0.3	-2.2;-0.1	-1.7;0.3	-1.9;0.5	P AvsC	0.546
	p-value#	0.005	0.032	0.152	0.234	P BvsC	0.99
	Median (IQR)	-0.8 (-2.5;0.8)	-1.2 (-3.1;0.8)	-0.8 (-2.4;0.8)	0 (-2.5;0.6)	P AvsB (Holm)	1
						P AvsC (Holm)	1
						P BvsC (Holm)	1
FGF-23							
Day 28 percentage change with respect to Baseline	N	69	23	24	22	P anova	0.835
	Mean (SD)	104.3 (241.4)	93.1 (190.6)	91.4 (174.9)	130.1 (340.7)	P AvsB	0.981
	95%CI	46.3;162.3	10.7;175.5	17.5;165.2	-20.9;281.2	P AvsC	0.613
	p-value#	0.001	0.029	0.018	0.088	P BvsC	0.592
	Median (IQR)	40.6 (-6.5;87.4)	26.7 (-31.9;118.2)	59.1 (10.1;92.5)	34.3 (-5.6;73.2)	P AvsB (Holm)	1
						P AvsC (Holm)	1
						P BvsC (Holm)	1
Day 56 percentage change with respect to Baseline	N	69	23	24	22	P anova	0.682
	Mean (SD)	121.5 (322.4)	140.4 (289.1)	74.9 (140.6)	152.5 (472.8)	P AvsB	0.492
	95%CI	44;198.9	15.4;265.5	15.5;134.3	-57.2;362.1	P AvsC	0.902
	p-value#	0.003	0.029	0.016	0.145	P BvsC	0.422
	Median (IQR)	27.3 (-30.8;142.9)	44.2 (-33.3;198.8)	17.9 (-16.8;123.1)	30.4 (-24.7;109.4)	P AvsB (Holm)	1
						P AvsC (Holm)	1
						P BvsC (Holm)	1
Day 84 percentage change with respect to Baseline	N	68	23	23	22	P anova	0.267
	Mean (SD)	90.6 (238.2)	156 (366.9)	49.5 (123.5)	65.3 (129.6)	P AvsB	0.132
	95%CI	32.9;148.3	-2.7;314.6	-3.9;102.9	7.8;122.7	P AvsC	0.204
	p-value#	0.003	0.054	0.068	0.028	P BvsC	0.824
	Median (IQR)	19.1 (-29.9;107.2)	17.9 (-36.5;149.9)	-1.7 (-42;100.2)	59.1 (-8.7;84.6)	P AvsB (Holm)	0.397
						P AvsC (Holm)	0.407
						P BvsC (Holm)	0.824
Day 112 percentage change with respect to Baseline	N	66	23	22	21	P anova	0.18
	Mean (SD)	164 (554.5)	114.8 (220.4)	43.4 (72.5)	344.2 (942.1)	P AvsB	0.664
	95%CI	27.7;300.3	19.4;210.1	11.2;75.5	-84.6;773	P AvsC	0.17
	p-value#	0.019	0.021	0.011	0.11	P BvsC	0.077
	Median (IQR)	50 (-8.5;108.5)	58.8 (-10.8;185)	42.6 (0.4;64)	50 (-21.9;137.7)	P AvsB (Holm)	0.664
						P AvsC (Holm)	0.341
						P BvsC (Holm)	0.23
CTX-I							
Day 28 percentage change with respect to Baseline	N	73	24	25	24	P anova	0.746
	Mean (SD)	12.8 (38.1)	8 (32.7)	16.3 (46.3)	14 (34.9)	P AvsB	0.458
	95%CI	3.9;21.7	-5.7;21.8	-2.8;35.3	-0.7;28.7	P AvsC	0.594
	p-value#	0.005	0.24	0.092	0.061	P BvsC	0.839
	Median (IQR)	8.6 (-5.9;25)	10.1 (-7.9;30)	8.6 (-4.4;24.1)	8 (-5.7;25.4)	P AvsB (Holm)	1
					-35;150	P AvsC (Holm)	1
						P BvsC (Holm)	1

Day 56 percentage change with respect to Baseline	N	73	24	25	24	P anova	0.611
	Mean (SD)	1.6 (48.7)	-3.5 (33.2)	9.5 (61.7)	-1.5 (47.4)	P AvsB	0.359
	95%CI	-9.7;13	-17.5;10.5	-16;34.9	-21.5;18.6	P AvsC	0.887
	p-value#	0.778	0.613	0.451	0.881	P BvsC	0.439
	Median (IQR)	-5.6 (-27.5;16.7)	4.3 (-21.6;9.9)	0 (-27.7;43.3)	-15.8 (-30.5;6.7)	P AvsB (Holm)	1
						P AvsC (Holm)	1
						P BvsC (Holm)	1
Day 84 percentage change with respect to Baseline	N	72	24	24	24	P anova	0.636
	Mean (SD)	5.7 (40)	4 (28.4)	11.9 (54.5)	1.3 (33.2)	P AvsB	0.496
	95%CI	-3.7;15.1	-8;16	-11.1;35	-12.8;15.3	P AvsC	0.816
	p-value#	0.229	0.5	0.294	0.855	P BvsC	0.362
	Median (IQR)	0 (-20.1;25)	4.5 (-6.7;23.9)	-4.5 (-24.6;28.8)	0 (-22.4;10.6)	P AvsB (Holm)	1
						P AvsC (Holm)	1
						P BvsC (Holm)	1
Day 112 percentage change with respect to Baseline	N	69	24	23	22	P anova	0.714
	Mean (SD)	1.5 (53.1)	-2.2 (34.4)	9 (58.1)	-2.4 (64.7)	P AvsB	0.477
	95%CI	-11.3;14.2	-16.7;12.3	-16.1;34.1	-31.1;26.3	P AvsC	0.99
	p-value#	0.817	0.759	0.466	0.865	P BvsC	0.479
	Median (IQR)	-7.3 (-32.5;17.6)	-2.9 (-23.3;18)	-2.6 (-32.4;23.2)	-17.6 (-38;0)	P AvsB (Holm)	1
						P AvsC (Holm)	1
						P BvsC (Holm)	1
P1NP							
Day 28 percentage change with respect to Baseline	N	73	24	25	24	P anova	0.624
	Mean (SD)	4.9 (17.2)	6.7 (20.2)	5.8 (15.2)	2.1 (16.1)	P AvsB	0.855
	95%CI	0.9;8.9	-1.9;15.2	-0.5;12	-4.7;8.9	P AvsC	0.362
	p-value#	0.018	0.12	0.069	0.531	P BvsC	0.459
	Median (IQR)	3 (-8.3;15.2)	3.8 (-2.6;14.6)	3 (-5.5;16.5)	2.6 (-10.8;9.5)	P AvsB (Holm)	1
						P AvsC (Holm)	1
						P BvsC (Holm)	1
Day 56 percentage change with respect to Baseline	N	73	24	25	24	P anova	0.313
	Mean (SD)	1 (18.4)	-3.6 (20.3)	2.5 (15.6)	4.2 (19)	P AvsB	0.253
	95%CI	-3.3;5.3	-12.2;5	-4;8.9	-3.9;12.2	P AvsC	0.148
	p-value#	0.638	0.394	0.439	0.296	P BvsC	0.747
	Median (IQR)	-1.1 (-11;14.5)	-7.8 (-15.7;8.5)	0.8 (-9.3;15.2)	7.1 (-8.2;15.4)	P AvsB (Holm)	0.506
						P AvsC (Holm)	0.445
						P BvsC (Holm)	0.747
Day 84 percentage change with respect to Baseline	N	72	24	24	24	P anova	0.556
	Mean (SD)	-2.4 (20.5)	-3 (21.8)	-5.3 (19)	1.1 (20.9)	P AvsB	0.703
	95%CI	-7.2;2.4	-12.2;6.2	-13.3;2.8	-7.7;9.9	P AvsC	0.493
	p-value#	0.324	0.506	0.187	0.799	P BvsC	0.287
	Median (IQR)	-3.8 (-14.7;11.3)	-5.6 (-14.6;7.9)	-7.5 (-19.9;10.8)	-0.5 (-8.4;21.1)	P AvsB (Holm)	0.985
						P AvsC (Holm)	0.985
						P BvsC (Holm)	0.86
Day 112 percentage change with respect to Baseline	N	69	24	23	22	P anova	0.769
	Mean (SD)	-7.1 (18)	-9.2 (16)	-6.3 (14.1)	-5.6 (23.5)	P AvsB	0.576
	95%CI	-11.4;-2.8	-16;-2.5	-12.3;-0.2	-16;4.8	P AvsC	0.503
	p-value#	0.002	0.01	0.044	0.275	P BvsC	0.908
	Median (IQR)	-8.6 (-17.6;3.5)	-8.7 (-20.3;4.1)	-8.6 (-14.4;3)	-8.8 (-17;3.5)	P AvsB (Holm)	1
						P AvsC (Holm)	1
						P BvsC (Holm)	1
BALP							
Day 28 percentage change with respect to Baseline	N	73	24	25	24	P anova	0.494
	Mean (SD)	-1.8 (15.6)	-0.4 (15.9)	-0.1 (12.1)	-4.9 (18.5)	P AvsB	0.951
	95%CI	-5.4;1.9	-7.1;6.3	-5.1;4.9	-12.7;2.9	P AvsC	0.321
	p-value#	0.333	0.905	0.962	0.207	P BvsC	0.288
	Median (IQR)	-1.7 (-10.7;7.9)	-1.3 (-8.2;7.6)	-2.8 (-8.9;8.1)	-6.7 (-15.4;5.3)	P AvsB (Holm)	0.951
						P AvsC (Holm)	0.865
						P BvsC (Holm)	0.865

Day 56 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	73 -4.4 (14.5) -7.8;-1 0.011 -2.4 (-15.4;5.2)	24 -3.5 (16.7) -10.5;3.5 0.316 -7.7 (-15.4;9)	25 -5.1 (13.5) -10.7;0.5 0.073 -2.4 (-8.9;3)	24 -4.7 (13.8) -10.5;1.1 0.109 -0.2 (-14;5.2)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.926 0.707 0.779 0.927 1 1 1
Day 84 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	72 -6.5 (16.7) -10.4;-2.6 0.001 -6.8 (-17.9;5.5)	24 -2.5 (18.2) -10.2;5.2 0.503 -2.2 (-16.1;9.9)	24 -10.1 (15.2) -16.5;-3.6 0.004 -8.5 (-23.6;-3.6)	24 -6.9 (16.3) -13.8;0 0.049 -11.1 (-17.1;5.5)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.296 0.122 0.365 0.514 0.365 0.731 0.731
Day 112 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	69 -10.0 (16.4) -14.5;-6.6 <0.001 -10.6 (-22.4;-1.1)	24 -9.4 (15.9) -16.1;-2.6 0.008 -8.3 (-21.8;-0.2)	23 -11.5 (17.5) -19;-3.9 0.005 -13 (-22.8;-3.3)	22 -11 (16.5) -18.3;-3.7 0.005 -10 (-20.6;-1.3)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.903 0.668 0.743 0.924 1 1 1
Dkk-1							
Day 28 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	73 15.6 (66.9) 0;31.2 0.05 -0.3 (-16.3;20.7)	24 28.9 (97.3) -12.2;70 0.159 9.1 (-8.1;42.4)	25 11 (48.7) -9.2;31.1 0.272 -4.4 (-16.5;18.8)	24 7.1 (42.1) -10.6;24.9 0.416 -4.5 (-22.3;21.2)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.489 0.352 0.265 0.842 0.794 0.794 0.842
Day 56 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	73 41.2 (76.4) 23.4;59.1 <0.001 21.7 (-3.3;60.8)	24 51.5 (104) 7.6;95.4 0.024 34.6 (1.4;53.8)	25 39.3 (59.3) 14.8;63.7 0.003 20.5 (-9.6;95.6)	24 33.1 (60) 7.7;58.4 0.013 14.9 (-1;58.5)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.703 0.582 0.411 0.779 1 1 1
Day 84 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	72 48.1 (77.6) 29.9;66.3 <0.001 18.5 (-2.5;80.7)	24 60.9 (94.3) 21.1;100.7 0.004 30.3 (2.9;81.2)	24 52.7 (73.2) 21.8;83.6 0.002 27.1 (0;86.7)	24 30.7 (62) 4.5;56.9 0.023 12.7 (-6.5;54.7)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.385 0.718 0.183 0.33 0.718 0.549 0.659
Day 112 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	69 46.1 (73.5) 28.5;63.8 <0.001 24.1 (-6;83.5)	24 51.2 (88) 14.1;88.4 0.009 17.8 (-5.3;93.8)	23 49.3 (72.2) 18.1;80.6 0.003 24.1 (0.3;78.2)	22 37.3 (58.6) 11.3;63.3 0.007 34.3 (-6.7;70.2)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.792 0.93 0.527 0.588 1 1 1
Sclerostin							
Day 28 percentage change with respect to Baseline	N Mean (SD) 95%CI p-value# Median (IQR)	73 -2.0 (47.6) -13.0;9.0 0.715 -7.5 (-35.9;35.4)	25 -5.1 (49.0) -25.3;15.1 0.608 -17 (-41.0;31.8)	24 -2.5 (40.8) -23.2;18.5 0.809 -7.6 (-42.0;33.0)	24 1.64 (44.4) -17.0;20.4 0.59 6.5 (-25.7;46.3)	P anova P AvsB P AvsC P BvsC P AvsB (Holm) P AvsC (Holm) P BvsC (Holm)	0.849 0.694 0.873 0.58 1 1 1

Day 56 percentage change with respect to Baseline	N	73	24	25	24	P anova	0.426
	Mean (SD)	8 (46.5)	-6.0 (52.3)	10.5 (35.47)	19.8 (48.7)	P AvsB	0.872
	95%CI	-13.1;9.0	-28.5;15.7	-4.1;25.2	(-0.8;40.3)	P AvsC	0.231
	p-value#	0.146	0.550	0.150	0.059	P BvsC	0.294
	Median (IQR)	-7.65 (-37.7;37.0)	-6.0 (-42.1;45.0)	2.1 (-13.4;35.3)	8.52 (-19.7;67.4)	P AvsB (Holm)	0.872
						P AvsC (Holm)	0.693
						P BvsC (Holm)	0.693
Day 84 percentage change with respect to Baseline	N	72	24	24	24	P anova	0.999
	Mean (SD)	4.7 (49.7)	-5.9 (49.4)	15.9 (9.8)	4.1 (53.1)	P AvsB	0.963
	95%CI	-3.0;20.4	-14.9;26.8	-4.27;36.2	-18.3;26.5	P AvsC	0.972
	p-value#	0.143	0.560	0.116	0.706	P BvsC	0.991
	Median (IQR)	2.5 (-32.2;50.0)	5.27 (-36.1;49.4)	9.9 (-29.4;52.0)	-6.1 (-35.6;51.1)	P AvsB (Holm)	1
						P AvsC (Holm)	1
						P BvsC (Holm)	1
Day 112 percentage change with respect to Baseline	N	69	24	23	22	P anova	0.404
	Mean (SD)	8.2 (35.8)	12.7 (36.2)	10.5 (38.1)	1.4 (33.4)	P AvsB	0.212
	95%CI	-0.02;16.4	-2.21;27.7	-5.2;26.2	-12.4;15.2	P AvsC	0.86
	p-value#	0.051	0.091	0.18	0.836	P BvsC	0.294
	Median (IQR)	10.8 (-21.2;33.3)	17.9 (-21.2;50.0)	5.8 (-13.8;31.6)	5.9 (-29.7;30.0)	P AvsB (Holm)	0.635
						P AvsC (Holm)	0.86
						P BvsC (Holm)	0.635

BALB = bone alkaline phosphatase; CTX-1 = C-terminal telopeptide of type I collagen; DKK-1 = Dickkopf-1; FGF-23 = fibroblast growth factor-23; IQR = interquartile range; P1NP = procollagen type I N-terminal propeptide; PTH = parathyroid hormone; SD = standard deviation
The Holm–Bonferroni method was used to counteract the problem of multiple comparisons.

