

ONLINE SUPPLEMENT

Supplemental Table 1. Baseline Characteristics of SPRINT participants with CKD by Serum Fibroblast Growth Factor 23				
	Quartiles			
	FGF23 Q1	FGF23 Q2	FGF23 Q3	FGF23 Q4
	n= 621	n=622	n=622	n=621
FGF23 range (pg/ml)	12.7-51.9	52.0-66.4	66.5-87.6	87.7-1687
Age (years) ± SD	73 (9)	74 (8)	73 (9)	73 (10)
Male, n (%)	389 (62.7)	392 (63.0)	363 (58.4)	343 (55.2)
Race, n (%)				
White	418 (67.3)	478 (76.9)	442 (71.1)	435 (70.1)
Black	184 (29.6)	130 (20.9)	160 (25.7)	175 (28.2)
Other	19 (3.1)	14 (2.3)	20 (3.2)	11 (1.8)
SPRINT CCN				
Utah	177 (28.5)	182 (29.3)	207 (33.3)	212 (34.1)
Ohio (Case Western)	94 (15.1)	87 (14.0)	95 (15.3)	99 (15.9)
Southeast (Wake)	122 (19.7)	111 (17.9)	103 (16.6)	115 (18.5)
South (Alabama)	103 (16.6)	119 (19.1)	94 (15.1)	78 (12.6)
Veterans Affairs	125 (20.1)	123 (19.8)	123 (19.8)	117 (18.8)
Prevalent Cardiovascular Disease, n (%)	142 (22.9)	161 (25.9)	164 (26.4)	158 (25.4)
Prevalent Heart Failure, n (%)	36 (5.8)	35 (5.6)	32 (5.1)	51 (8.3)
eGFR (ml/min/1.73m ²) ± SD	50 (8)	49 (8)	46 (9)	39 (12)
eGFR Categories, n (%)				
45-59 ml/min/1.73m ²	474 (76.3)	441 (70.9)	352 (56.6)	204 (32.9)
30-44 ml/min/1.73m ²	131 (21.1)	168 (27.0)	231 (37.1)	245 (39.45)
< 30 ml/min/1.73m ²	16 (2.6)	13 (2.1)	39 (6.3)	172 (27.7)
Urine Albumin/Creatinine, Median [IQR]	13 [7-37]	12 [6-33]	17 [7-59]	24 [10-99]
Urine Albumin/Creatinine > 30 mg/g, n (%)	176 (29)	162 (27)	221 (36)	269 (44)
Systolic BP (mm Hg) ± SD	141 (17)	140 (16)	139 (17)	139 (17)
Diastolic BP (mm Hg) ± SD	76 (13)	75 (12)	74 (13)	73 (13)

# of Antihypertensives	2.0	2.1	2.2	2.3
Smoking, n (%)				
Current	85 (13.7)	39 (6.3)	43 (6.9)	52 (8.4)
Former	270 (43.5)	288 (46.3)	294 (47.3)	285 (45.9)
Never	266 (42.8)	295 (47.4)	295 (45.8)	284 (45.7)
Body mass index (kg/m ²) ± SD	29.2 (5.9)	29.2 (5.2)	30.0 (6.0)	29.7 (6.4)
Total cholesterol (mg/dl) ± SD	181 (40)	184 (40)	184 (41)	186 (42)
HDL cholesterol (mg/dl) ± SD	53 (15)	52 (14)	52 (14)	53 (15)
Calcium (mg/dl) ± SD	9.5 (0.4)	9.6 (0.5)	9.6 (0.5)	9.7 (0.5)
Phosphate (mg/dl) ± SD	3.4 (0.5)	3.5 (0.5)	3.6 (0.5)	3.7 (0.6)
Parathyroid hormone (pg/ml), median [IQR]	46 [34-61]	44 [34-59]	48 [36-67]	55 [37-83]

Supplemental Table 2. Association of Serum PTH with Cardiovascular Composite Endpoints in SPRINT Participants with CKD

	PTH Q1	PTH Q2	PTH Q3	PTH Q4	Per Doubling of PTH	P Value	P-Interaction*
Range (pg/ml)	4-35	36-48	49-67	68-409			
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)		
MI							
Model 1	Reference	0.78 (0.42, 1.50)	1.00 (0.54, 1.87)	1.63 (0.92, 2.89)	1.49 (1.11, 2.03)	0.009	
Model 2	Reference	0.74 (0.39, 1.45)	0.85 (0.43, 1.67)	1.43 (0.77, 2.67)	1.41 (1.01, 1.99)	0.05	0.64
Non MI ACS							
Model 1	Reference	0.37 (0.09,1.38)	1.40 (0.55,3.56)	1.07 (0.39,3.01)	1.37 (0.80, 2.35)	0.25	
Model 2	Reference	0.35 (0.09, 1.35)	1.28 (0.48, 3.39)	0.73 (0.22, 2.43)	1.17 (0.63, 2.16)	0.61	0.76
Stroke							
Model 1	Reference	1.69 (0.74, 3.83)	1.86 (0.80, 4.26)	2.49 (1.11, 5.53)	1.63 (1.13, 2.33)	0.008	
Model 2	Reference	1.63 (0.69, 3.87)	1.82 (0.76, 4.34)	1.97 (0.81, 4.76)	1.45 (0.97, 2.16)	0.07	0.9
CVD Death							
Model 1	Reference	1.13 (0.44, 2.87)	1.48 (0.59,3.70)	2.83 (1.23, 6.49)	1.94 (1.31, 2.87)	0.001	
Model 2	Reference	0.69 (0.24, 1.92)	1.00 (0.39, 2.55)	1.337 (0.57, 3.33)	1.29 (0.84, 1.97)	0.24	0.49

Model 1: Adjusted for age, gender, race, and randomized treatment arm

Model 2: Adjusted for Model 1 variables plus eGFR-Creatinine-Cystatin C, urine albumin-creatinine ratio, prevalent cardiovascular disease, prevalent heart failure, systolic blood pressure, # antihypertensives at baseline, smoking, body mass index, Total cholesterol and HDL cholesterol

* P-interaction for interaction between serum PTH and treatment arm.

Supplemental Table 3. Effects of Randomization to the Intensive vs. Standard BP arms, Stratified by Serum Fibroblast Growth Factor 23 Levels Above vs. Below the Median in CKD Participants in SPRINT*

Standard			Intensive		P-Interaction**
	# Events / # At Risk	HR (95% CI)	# Events / # At Risk	HR (95% CI)	
Cardiovascular Events					0.48
≤ Median	64/564	Reference	56/628	0.81 (0.56, 1.18)	
> Median	77/605	Reference	64/585	0.88 (0.62, 1.25)	
Heart Failure					0.06
≤ Median	20/564	Reference	16/628	0.74 (0.37, 1.48)	
> Median	39/605	Reference	27/585	0.66 (0.39, 1.12)	

*Models adjusted for age, gender, race, eGFR-Creatinine-Cystatin C, and urine albumin-creatinine ratio,

prevalent cardiovascular disease, prevalent heart failure, systolic blood pressure, # antihypertensives at

baseline, smoking, body mass index, Total cholesterol and HDL cholesterol

** Interaction p-value evaluating parathyroid hormone as a continuous variable.

Supplemental Table 4. Association of Serum Fibroblast Growth Factor 23 with Cardiovascular Composite Endpoints in SPRINT Participants with CKD

	FGF23 Q1	FGF23 Q2	FGF23 Q3	FGF23 Q4	Per Doubling of FGF	P Value	P Int*
Range (pg/ml)	13-52	52-66	67-88	88-1687			
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)		
MI							
Model 1	Reference	1.01 (0.53, 1.94)	1.34 (0.73, 2.48)	1.50 (0.72, 2.48)	1.32 (0.96, 1.82)	0.09	
Model 2	Reference	1.15 (0.57, 2.31)	1.29 (0.66, 2.53)	1.34 (0.65, 2.78)	1.15 (0.78, 1.69)	0.48	0.32
Non MI ACS							
Model 1	Reference	1.12 (0.37, 3.34)	1.49 (0.53, 4.19)	1.08 (0.35, 3.37)	0.93 (0.50, 1.75)	0.84	
Model 2	Reference	1.35 (0.38, 4.86)	2.15 (0.64, 7.21)	1.74 (0.44, 6.88)	1.33 (0.63, 2.82)	0.45	0.79
Stroke							
Model 1	Reference	1.22 (0.59, 2.55)	0.95 (0.43, 2.09)	1.59 (0.78, 3.22)	1.37 (0.93, 2.00)	0.11	
Model 2	Reference	1.39 (0.63, 3.03)	0.98 (0.41, 2.28)	1.34 (0.57, 3.14)	1.23 (0.79, 1.94)	0.35	0.43
CVD Death							
Model 1	Reference	0.89 (0.36, 2.20)	1.24 (0.54, 2.93)	2.12 (0.98, 4.59)	1.69 (1.16, 2.45)	0.006	
Model 2	Reference	0.90 (0.35, 2.31)	0.78 (0.31, 1.97)	0.82 (0.32, 2.10)	0.97 (0.57, 1.65)	0.92	0.5

Model 1: Adjusted for age, gender, race, and randomized treatment arm

Model 2: Adjusted for Model 1 variables plus eGFR-Creatinine-Cystatin C, urine albumin-creatinine ratio, prevalent cardiovascular disease, prevalent heart failure, systolic blood pressure, # antihypertensives at baseline, smoking, body mass index, Total cholesterol and HDL cholesterol

* P-interaction for interaction between serum PTH and treatment arm.

Supplemental Table 5. Association of Serum PTH/FePhos with Cardiovascular Events, Heart Failure Events, and Mortality in SPRINT Participants with CKD

Range (pg/ml)	PTH/FePhos Q1 0.23-1.93	PTH/FePhos Q2 1.93-2.80	PTH/FePhos Q3 2.80-4.19	PTH/FePhos Q4 4.19-67.4	P Value	Per Doubling of PTH/FePhos HR (95% CI)	P Value
Cardiovascular Events							
# Events/ # At Risk (%)	51/528 (9.7%)	61/515 (11.8%)	59/496 (11.9%)	47/488 (9.6%)			
Model 1	Reference	1.31 (0.89, 1.93)	1.44 (0.97, 2.15)	1.24 (0.80, 1.93)	0.53	1.11 (0.94, 1.31)	0.24
Model 2	Reference	1.32 (0.89, 1.96)	1.50 (1.00, 2.27)	1.18 (0.75, 1.85)	0.23	1.10 (0.93, 1.300)	0.25
Heart Failure							
# Events/ # At Risk (%)	19/528 (3.6%)	21/515 (4.1%)	25/496 (5.0%)	24/488 (4.9%)			
Model 1	Reference	1.04 (0.54, 2.00)	1.25 (0.66, 2.38)	1.23 (0.62, 2.43)	0.88	1.04 (0.80, 1.36)	0.75
Model 2	Reference	0.96 (0.49, 1.89)	1.21 (0.62, 2.38)	1.06 (0.52, 2.17)	0.91	1.02 (0.78, 1.33)	0.89
All-Cause Mortality							
# Events/ # At Risk (%)	36/528 (6.8%)	35/515 (6.8%)	44/496 (8.9%)	37/488 (7.6%)			
Model 1	Reference	1.16 (0.71, 1.89)	1.47 (0.92, 2.35)	1.27 (0.75, 2.13)	0.45	1.13 (0.92, 1.38)	0.25
Model 2	Reference	1.17 (0.71, 1.92)	1.44 (0.89, 2.33)	1.22 (0.71, 2.08)	0.54	1.11 (0.91, 1.36)	0.32

Model 1: Adjusted for age, gender, race, and randomized treatment arm

Model 2: Adjusted for Model 1 variables plus eGFR-Creatinine-Cystatin C, urine albumin-creatinine ratio, prevalent cardiovascular disease, prevalent heart failure, systolic blood pressure, # antihypertensives at baseline, smoking, body mass index, Total cholesterol and HDL cholesterol

Supplemental Table 6. Association of iPTH/FeCa with CVD Events, HF Events, and Mortality in SPRINT Participants with CKD

Range (pg/ml)	PTH/FeCa Q1 3.59-43.8	PTH/FeCa Q2 43.8-99.9	PTH/FeCa Q3 99.9-242.6	PTH/FeCa Q4 242.6-2746	P Value	Per Doubling of PTH/FeCa HR (95% CI)	P Value
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)			
Cardiovascular Events							
# Events/ # At Risk (%)	50/487 (10.3%)	48/494 (9.7%)	54/514 (10.5%)	66/532 (12.4%)			
Model 1	Reference	0.99 (0.65, 1.49)	1.18 (0.79, 1.77)	1.47 (0.99, 2.19)	0.16	1.07 (0.99, 1.64)	0.11
Model 2	Reference	0.97 (0.64, 1.49)	1.17 (0.77, 1.78)	1.27 (0.84, 1.92)	0.55	1.04 (0.95, 1.13)	0.37
Heart Failure							
# Events/ # At Risk (%)	21/487 (4.3%)	14/494 (2.8%)	23/514 (4.5%)	31/532 (5.8%)			
Model 1	Reference	0.70 (0.34, 1.42)	1.25 (0.67, 2.36)	1.49 (0.81, 2.77)	0.14	1.11 (0.98, 1.26)	0.11
Model 2	Reference	0.71 (0.33, 1.47)	1.26 (0.64, 2.49)	1.19 (0.62, 2.33)	0.39	1.05 (0.92, 1.20)	0.47
All-Cause Mortality							
# Events/ # At Risk (%)	32/487 (6.6%)	38/494 (7.7%)	33/514 (6.4%)	49/532 (9.2%)			
Model 1	Reference	1.24 (0.76, 2.04)	1.12 (0.67, 1.88)	1.36 (0.84, 2.23)	0.63	1.04 (0.94, 1.15)	0.42
Model 2	Reference	1.22 (0.74, 2.04)	1.06 (0.63, 1.81)	1.10 (0.66, 1.83)	0.89	1.00 (0.90, 1.11)	0.98

Model 1: Adjusted for age, gender, race, and randomized treatment arm

Model 2: Adjusted for Model 1 variables plus eGFR-Creatinine-Cystatin C, urine albumin-creatinine ratio, prevalent cardiovascular disease, prevalent heart failure, systolic blood pressure, # antihypertensives at baseline, smoking, body mass index, Total cholesterol and HDL cholesterol

Supplemental Table 7. Association of FGF-23/FePhos with CVD Events, HF Events, and Mortality in SPRINT Participants with CKD

	FGF23/FePhos Q1	FGF23/FePhos Q2	FGF23/FePhos Q3	FGF23/FePhos Q4		Per Doubling of	
Range (pg/ml)	0.23-2.83	2.83-3.93	3.93-5.49	5.49-155.1	P	FGF23/FePhos	P
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	Value	HR (95% CI)	Value
Cardiovascular Events							
# Events/ # At Risk (%)	59/519 (27.1%)	70/514 (32.1%)	50/521 (9.6%)	39/472 (8.3%)			
Model 1	Reference	1.17 (0.82, 1.69)	0.91 (0.61, 1.35)	0.85 (0.55, 1.32)	0.42	0.91 (0.76, 1.09)	0.31
Model 2	Reference	1.04 (0.72, 1.51)	0.88 (0.58, 1.31)	0.84 (0.53, 1.31)	0.72	0.90 (0.74, 1.08)	0.25
Heart Failure							
# Events/ # At Risk (%)	24/519 (4.6%)	30/514 (5.8%)	21/521 (4.0%)	14/472 (3.0%)			
Model 1	Reference	1.24 (0.71, 2.21)	0.88 (0.47, 1.64)	0.59 (0.28, 1.20)	0.17	0.73 (0.55, 0.97)	0.03
Model 2	Reference	1.05 (0.59, 1.91)	0.74 (0.38, 1.44)	0.58 (0.27, 1.20)	0.32	0.70 (0.52, 0.95)	0.02
All-Cause Mortality							
# Events/ # At Risk (%)	41/519 (7.9%)	37/514 (7.2%)	44/521 (8.5%)	30/472 (6.4%)			
Model 1	Reference	0.87 (0.55, 1.38)	1.17 (0.75, 1.84)	1.02 (0.60, 1.70)	0.64	1.11 (0.89, 1.38)	0.35
Model 2	Reference	0.72 (0.45, 1.16)	1.13 (0.71, 1.79)	0.88 (0.52, 1.48)	0.29	1.05 (0.84, 1.31)	0.67

Model 1: Adjusted for age, gender, race, and randomized treatment arm

Model 2: Adjusted for Model 1 variables plus eGFR-Creatinine-Cystatin C, urine albumin-creatinine ratio, prevalent cardiovascular disease, prevalent heart failure, systolic blood pressure, # antihypertensives at baseline, smoking, body mass index, Total cholesterol and HDL cholesterol

Supplemental Table 8. Association of Parathyroid Hormone and Fibroblast Growth Factor 23 with Serious Adverse Events in SPRINT Participants with CKD

	PTH≤ Median	PTH>Median	FGF23≤ Median	FGF23>Median
Any SAE, n (%)	629 (49)	648 (53)	591 (48)	686 (54)
Hypotension, n (%)	35 (3)	47 (4)	37 (3)	45 (4)
AKI, n (%)	78 (6)	124 (10)	86 (7)	116 (9)
Syncope, n (%)	44 (3)	30 (2)	41 (3)	33 (3)
Fall, n (%)	62 (5)	45 (4)	39 (3)	68 (5)
Electrolyte, n (%)	57 (4)	55 (4)	50 (4)	62 (5)
Bradycardia, n (%)	41 (3)	42(3)	30 (2)	53 (4)