Table S 1 Baseline characteristics of study participants after stratification by tertiles of sKlotho

	Tertile 1 n=148 (171-358 pg/ml)	Tertile 2 n=148 (359-444 pg/ml)	Tertile 3 n=148 (446-2054 pg/ml)	p
Age (years)	67 ± 11	65 ± 11	63 ± 14	0.02
Women	54 (37 %)	63 (43 %)	62 (42 %)	0.51
Smokers	16 (11 %)	14 (9 %)	14 (9 %)	0.90
Diabetes mellitus	55 (37 %)	53 (36 %)	60 (50 %)	0.69
Prevalent CVD	51 (34 %)	41 (28 %)	43 (29 %)	0.41
CRP (mg/l)	2.9 (1.4-6.0)	2.9 (1.1-5.6)	2.4 (1.1-4.4)	0.01
Total cholesterol (mg/dl)	195 ± 40	190 ± 40	194 ± 46	0.58
HDL-C (mg/dl)	51 ± 17	53 ± 18	51 ± 17	0.35
LDL-C (mg/dl)	119 ± 34	112 ± 35	116 ± 36	0.16
BMI (kg/m^2)	30 ± 5	30 ± 6	30 ± 6	0.85

	Tertile 1 n=148 (171-358 pg/ml)	Tertile 2 n=148 (359-444 pg/ml)	Tertile 3 n=148 (446-2054 pg/ml)	p
Calcium (mmol/l)	2.4 ± 0.1	2.4 ± 0.1	2.4 ± 0.1	0.70
Phosphate (mg/dl)	3.5 ± 0.7	3.4 ± 0.8	3.3 ± 0.6	0.24
FGF-23 (rU/ml)	107 (70-193)	103 (60-150)	89 (60-151)	0.85
sKlotho (pg/ml)	296 (260-326)	397 (375-425)	565 (484-664)	<0.001
PTH (pg/ml)	52 (35-85)	54 (38-88)	54 (38-78)	0.70
eGFR (ml/min/1.73 m²)	42 ± 14	46 ± 18	47 ± 15	0.009
UAE (mg/g creatinine)	30 (7-177)	27 (6-198)	51 (15-206)	0.32
FePi	26 ± 13 %	25 ± 13 %	26 ± 13 %	0.58
BB intake	107 (72 %)	104 (70 %)	90 (61 %)	0.08
ACE-I intake	55 (37 %)	53 (36 %)	57 (39 %)	0.89
Statin intake	77 (52 %)	78 (53 %)	61 (41 %)	0.09

	Tertile 1 n=148 (171-358 pg/ml)	Tertile 2 n=148 (359-444 pg/ml)	Tertile 3 n=148 (446-2054 pg/ml)	p
unhydroxylated Vitamin D_3 intake	66 (45 %)	62 (42 %)	61 (41 %)	0.82
active Vitamin D_3 intake	15 (10 %)	8 (5 %)	10 (7 %)	0.28

Abbreviations: CVD, cardiovascular disease; CRP, C-reactive protein; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol, BMI, body mass index; FGF-23, Fibroblast Growth Factor-23; sKlotho, soluble Klotho; PTH, parathyroid hormone; eGFR, estimated glomerular filtration rate; UAE, urinary albumin excretion; FePi, urinary fractional phosphate excretion; BB, beta blocker; ACE-I, angiotensin converting enzyme inhibitor. Variables are depicted as numbers of patients (percentage), as mean value ± standard deviation, or as median (interquartile range), as appropriate.

Table S 2 Baseline characteristics of study participants after stratification by tertiles of FGF-23

	Tertile 1 n = 148 (14.8-72.9 rU/ml)	Tertile 2 n = 148 (73.3-139.3 rU/ml)	Tertile 3 n=148 (139.8-7441.8 rU/ml)	p
Age (years)	62 ± 12	65 ± 14	65 ± 12	<0.001
Women	53 (36 %)	62 (42 %)	64 (43 %)	0.38
Smokers	15 (10 %)	11 (7 %)	18 (12 %)	0.39
Diabetes mellitus	47 (32 %)	56 (38 %)	65 (44 %)	0.10
Prevalent CVD	34 (23 %)	47 (32 %)	54 (36 %)	0.04
CRP (mg/l)	2.3 (1.0-5.1)	2.4 (1.1-4.4)	3.9 (1.4-8.0)	<0.001
Total cholesterol (mg/dl)	194 ± 41	196 ± 43	189 ± 42	0.26
HDL-C (mg/dl)	54 ± 19	51 ± 17	49 ± 16	0.03
LDL-C (mg/dl)	118 ± 35	116 ± 36	116 ± 35	0.50
BMI (kg/m^2)	30 ± 6	30 ± 5	30 ± 6	0.92
Calcium (mmol/l)	2.4 ± 0.1	2.4 ± 0.1	2.4 ± 0.1	0.45

	Tertile 1 n = 148 (14.8-72.9 rU/ml)	Tertile 2 n = 148 (73.3-139.3 rU/ml)	Tertile 3 n=148 (139.8-7441.8 rU/ml)	p
Phosphate (mg/dl)	3.2 ± 0.5	3.3 ± 0.8	3.7 ± 0.7	<0.001
FGF-23 (rU/ml)	53 (41-64)	101 (88-117)	205 (163-337)	<0.001
sKlotho (pg/ml)	418 (344-550)	384 (339-450)	388 (303-466)	0.07
PTH (pg/ml)	45 (33-58)	53 (38-78)	74 (47-134)	<0.001
eGFR (ml/min/1.73 m²)	55 ± 12	47 ± 14	33 ± 13	<0.001
UAE (mg/g creatinine)	18 (5-67)	31 (8-150)	100 (22-505)	0.001
FePi (%)	20 ± 9	24 ± 12	33 ± 14	<0.001
BB intake	81 (55 %)	109 (74 %)	111 (75 %)	<0.001
ACE-I intake	48 (32 %)	63 (43 %)	54 (36 %)	0.19
Statin intake	63 (43 %)	77 (52 %)	76 (51 %)	0.19
unhydroxylated Vitamin D_3 intake	48 (32 %)	63 (43 %)	78 (53 %)	0.002
activeVitamin D_3 intake	2 (1 %)	4 (3 %)	27 (18 %)	<0.001

Abbreviations: CVD, cardiovascular disease; CRP, C-reactive protein; HDL-C: high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol, BMI, body mass index; FGF-23, Fibroblast Growth Factor-23; sKlotho, soluble Klotho; PTH, parathyroid hormone; eGFR, estimated glomerular filtration rate; UAE, urinary albumin excretion; FePi, urinary fractional phosphate excretion; BB, beta blocker; ACE-I, angiotensin converting enzyme inhibitor. Variables are depicted as numbers of patients (percentage), as mean value ± standard deviation, or as median (interquartile range), as appropriate.

Table S 3 Cox regression analysis: Atherosclerotic events / death with categorized independent variables

	Univariate analysis			Adjustment for eGFR and ln albuminuria			Adjustment for eGFR, ln albuminuria, age and gender			Adjustment for eGFR, ln albuminuria, age, gender, diabetes mellitus and CVD			Adjustment for eGFR, ln albuminuria, age, gender, diabetes mellitus, CVD and CKD-MBD* parameters		
	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p
sKlotho (pg/ml)															
Tertile 1	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-
Tertile 2	0.72	0.42-1.25	0.25	0.82	0.47-1.42	0.48	0.84	0.49-1.46	0.54	0.70	0.40-1.22	0.21	0.69	0.39-1.22	0.20
Tertile 3	0.75	0.44-1.29	0.30	0.83	0.48-1.43	0.50	0.85	0.49-1.47	0.56	0.75	0.43-1.29	0.30	0.75	0.43-1.30	0.30
FGF-23 (rU/ml)															
Tertile 1	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-
Tertile 2	1.78	0.94-3.38	0.08	1.33	0.68-2.60	0.40	1.56	0.80-3.04	0.19	1.58	0.81-3.06	0.18	1.53	0.79-2.97	0.21
Tertile 3	2.58	1.42-4.70	0.002	1.28	0.61-2.72	0.52	1.27	0.59-2.71	0.54	1.24	0.59-2.62	0.57	1.23	0.58-2.61	0.59

* Ln sKlotho, PTH, FePi, phosphate and / or Ln FGF-23, as appropriate

Abbreviations: sKlotho, soluble Klotho; PTH, parathyroid hormone; FePi, urinary fractional phosphate excretion; FGF-23, Fibroblast Growth Factor-23; eGFR, estimated glomerular filtration rate; CVD: prevalent cardiovascular disease. Presented are hazard ratio (HR), 95% confidence interval (CI) and levels of significance (p).

Table S 4 Cox regression analysis: decompensated heart failure / death with categorized variables

	Univariate analysis			Adjustment for eGFR and ln albuminuria			Adjustment for eGFR, ln albuminuria, age and gender			Adjustment for eGFR, ln albuminuria, age, gender, diabetes mellitus and CVD			Adjustment for eGFR, ln albuminuria, age, gender, diabetes mellitus, CVD and CKD-MBD* parameters		
	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p
sKlotho (pg/ml)															
Tertile 1	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-
Tertile 2	0.64	0.31-1.34	0.24	0.70	0.33-1.47	0.34	0.70	0.33-1.47	0.35	0.60	0.28-1.28	0.19	0.50	0.23-1.08	0.08
Tertile 3	0.80	0.40-1.60	0.52	0.92	0.45-1.85	0.81	0.96	0.47-1.95	0.91	0.87	0.43-1.78	0.71	0.81	0.39-1.66	0.56
FGF-23 (rU/ml)															
Tertile 1	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-
Tertile 2	3.07	0.99-9.52	0.05	2.54	0.79-8.12	0.12	2.92	0.92-9.27	0.07	2.83	0.89-9.01	0.08	2.86	0.90-9.12	0.08
Tertile 3	7.32	2.57-20.87	<0.001	4.67	1.40-15.61	0.01	5.03	1.49-16.94	0.009	4.77	1.42-15.99	0.01	4.51	1.33-15.21	0.02

* Ln sKlotho, PTH, FePi, phosphate and / or Ln FGF-23, as appropriate

Abbreviations: sKlotho, soluble Klotho; PTH, parathyroid hormone; FePi, urinary fractional phosphate excretion; FGF-23, Fibroblast Growth Factor-23; eGFR, estimated glomerular filtration rate; CVD: prevalent cardiovascular disease. Presented are hazard ratio (HR), 95% confidence interval (CI) and levels of significance (p).

Table S 5 Cox regression analysis: Decompensated heart failure

	Univariate analysis			Adjustment for eGFR and ln albuminuria			Adjustment for eGFR, ln albuminuria, age and gender			Adjustment for eGFR, ln albuminuria, age, gender, diabetes mellitus and CVD			Adjustment for eGFR, ln albuminuria, age, gender, diabetes mellitus, CVD and CKD-MBD* parameters		
	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p
Ln sKlotho (pg/ml)	0.95	0.27-3.40	0.94	1.24	0.35-4.38	0.74	1.15	0.36-3.64	0.81	1.06	0.31-3.66	0.92	1.02	0.29-3.65	0.97
PTH (pg/ml)	1.01	1.00-1.01	0.001	1.00	1.00-1.01	0.28	1.00	1.00-1.01	0.26	1.00	1.00-1.01	0.16	1.00	1.00-1.01	0.38
FePi (%)	1.04	1.01-1.07	0.003	1.01	0.98-1.05	0.54	1.01	0.97-1.05	0.71	1.01	0.96-1.05	0.81	1.02	0.97-1.07	0.56
Phosphate (mg/dl)	1.65	1.21-2.25	0.002	1.37	0.90-2.09	0.15	1.39	0.88-2.20	0.16	1.54	0.95-2.49	0.07	1.59	0.87-2.93	0.14
Ln FGF-23 (rU/ml)	2.35	1.71-3.23	<0.001	2.03	1.38-3.01	<0.001	1.81	1.24-2.64	0.002	1.74	1.18-2.56	0.005	1.62	1.08-2.43	0.02

* Ln sKlotho, PTH, FePi, phosphate and / or Ln FGF-23, as appropriate

Abbreviations: sKlotho, soluble Klotho; PTH, parathyroid hormone; FePi, urinary fractional phosphate excretion; FGF-23, Fibroblast Growth Factor-23; eGFR, estimated glomerular filtration rate; CVD: prevalent cardiovascular disease. Presented are hazard ratio (HR), 95% confidence interval (CI) and levels of significance (p).

Table S 6 Cox regression analysis: Total mortality

	Univariate analysis			Adjustment for eGFR and ln albuminuria			Adjustment for eGFR, ln albuminuria, age and gender			Adjustment for eGFR, ln albuminuria, age, gender, diabetes mellitus and CVD			Adjustment for eGFR, ln albuminuria, age, gender, diabetes mellitus, CVD and CKD-MBD* parameters		
	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p
Ln sKlotho (pg/ml)	1.75	0.58-5.24	0.32	1.94	0.65-5.79	0.24	1.67	0.62-4.53	0.31	1.65	0.57-4.75	0.36	1.54	0.52-4.58	0.44
PTH (pg/ml)	1.01	1.00-1.01	0.01	1.00	1.00-1.01	0.34	1.00	1.00-1.01	0.28	1.00	1.00-1.01	0.16	1.00	1.00-1.01	0.25
FePi (%)	1.04	1.01-1.06	0.003	1.02	0.99-1.06	0.20	1.02	0.98-1.06	0.32	1.02	0.98-1.06	0.38	1.01	0.97-1.05	0.72
Phosphate (mg/dl)	1.16	0.76-1.79	0.50	0.86	0.51-1.43	0.56	0.83	0.47-1.45	0.51	0.89	0.50-1.59	0.70	0.81	0.42-1.57	0.53
Ln FGF-23 (rU/ml)	2.13	1.66-2.72	<0.001	1.86	1.37-2.54	<0.001	1.71	1.27-2.29	<0.001	1.66	1.24-2.24	0.001	1.60	1.17-2.18	0.003

* Ln sKlotho, PTH, FePi, phosphate and / or Ln FGF-23, as appropriate

Abbreviations: sKlotho, soluble Klotho; PTH, parathyroid hormone; FePi, urinary fractional phosphate excretion; FGF-23, Fibroblast Growth Factor-23; eGFR, estimated glomerular filtration rate; CVD: prevalent cardiovascular disease. Presented are hazard ratio (HR), 95% confidence interval (CI) and levels of significance (p).

Table S 7 Cox regression analysis: Atherosclerotic events

	Univariate analysis			Adjustment for eGFR and ln albuminuria			Adjustment for eGFR, ln albuminuria, age and gender			Adjustment for eGFR, ln albuminuria, age, gender, diabetes mellitus and CVD			Adjustment for eGFR, ln albuminuria, age, gender, diabetes mellitus, CVD and CKD-MBD* parameters		
	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p
Ln sKlotho (pg/ml)	0.68	0.32-1.44	0.31	0.81	0.38-1.70	0.58	0.78	0.38-1.59	0.49	0.59	0.28-1.26	0.17	0.60	0.28-1.26	0.18
PTH (pg/ml)	1.00	1.00-1.01	0.006	1.00	1.00-1.00	0.81	1.00	1.00-1.00	0.82	1.00	1.00-1.00	0.83	1.00	1.00-1.00	0.84
FePi (%)	1.03	1.02-1.05	<0.001	1.01	1.00-1.03	0.37	1.01	0.98-1.03	0.72	1.00	0.97-1.02	0.82	1.00	0.98-1.03	0.77
Phosphate (mg/dl)	1.40	1.12-1.78	0.005	1.09	0.81-1.47	0.57	1.09	0.80-1.49	0.59	1.21	0.87-1.68	0.26	1.22	0.85-1.75	0.29
Ln FGF-23 (rU/ml)	1.51	1.21-1.89	<0.001	1.11	0.82-1.51	0.49	1.08	0.80-1.45	0.63	1.05	0.79-1.40	0.74	1.04	0.77-1.40	0.80

* Ln sKlotho, PTH, FePi, phosphate and / or Ln FGF-23, as appropriate

Abbreviations: sKlotho, soluble Klotho; PTH, parathyroid hormone; FePi, urinary fractional phosphate excretion; FGF-23, Fibroblast Growth Factor-23; eGFR, estimated glomerular filtration rate; CVD: prevalent cardiovascular disease. Presented are hazard ratio (HR), 95% confidence interval (CI) and levels of significance (p).

Figure legend

Figure S1: FGF-23 tertiles and event-free survival from decompensated heart failure / death in the (a) lowest, (b) intermediate and (c) highest tertile of sKlotho (Kaplan-Meier analysis with log-rank test).
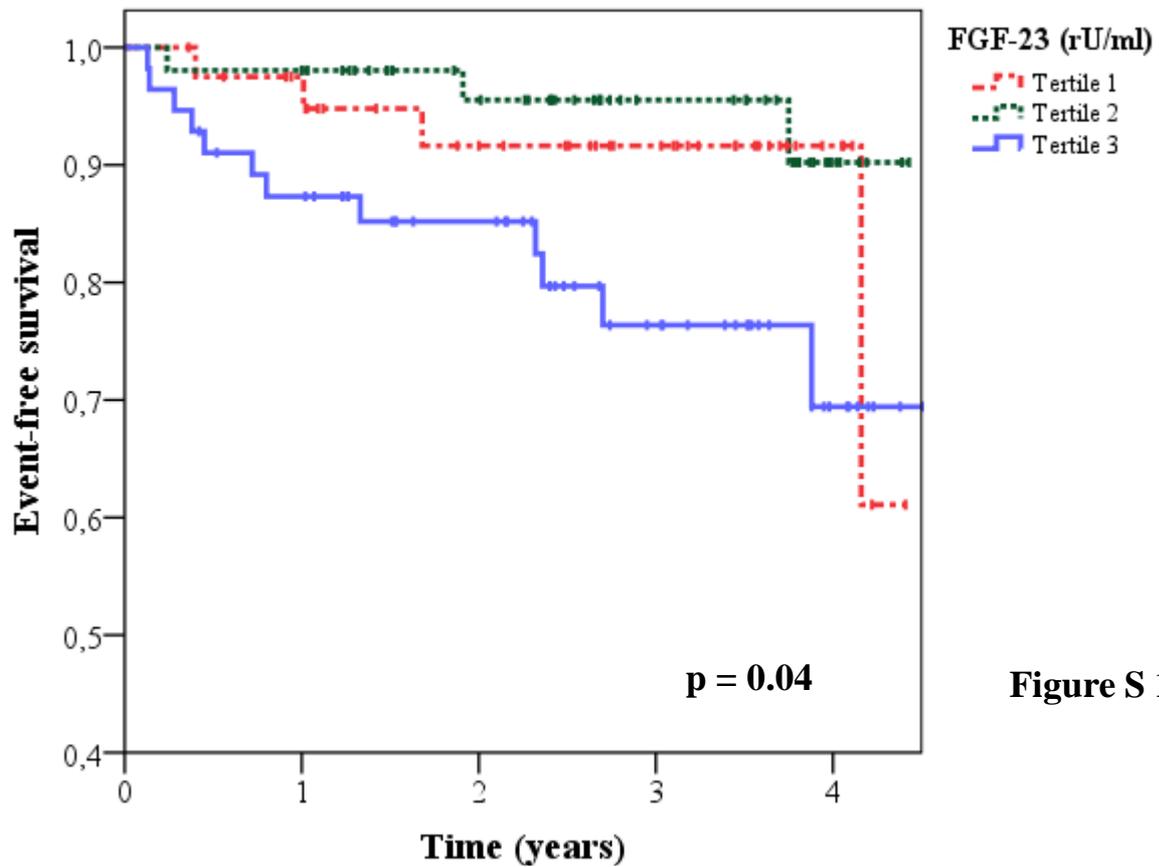
Figure S 1 a

Number at risk				
Tertile 1	35	27	19	5
Tertile 2	49	37	22	5
Tertile 3	46	35	20	6

p = 0.02
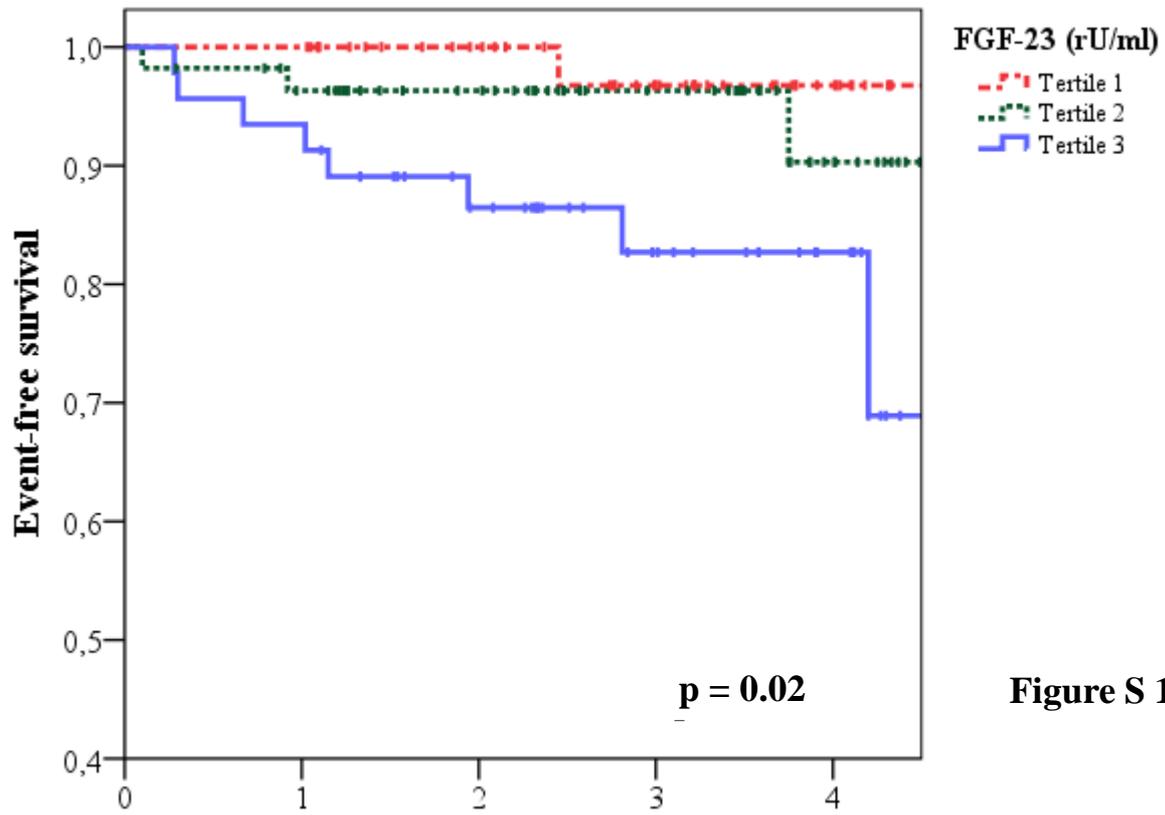
Figure S 1 b

Number at risk				
Tertile 1	45	34	24	10
Tertile 2	49	38	25	9
Tertile 3	42	31	19	10
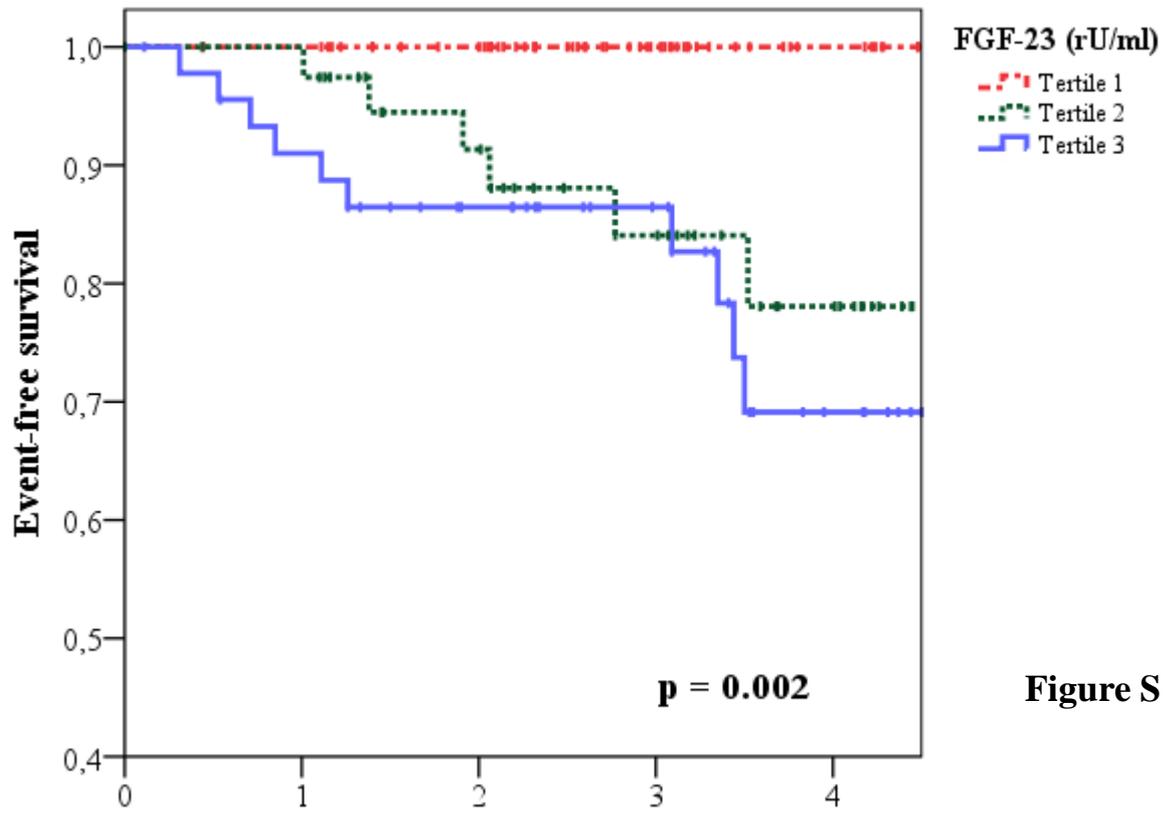
Figure S 1 c

Number at risk

Tertile 1	59	51	27	11
Tertile 2	38	28	19	9
Tertile 3	39	31	23	10