

Table S1: Comparison of Characteristics in the Sub-cohort versus All of FAVORIT

	Sub-cohort	Whole cohort
N	491	4110
Age \pm SD	51 \pm 9	52 \pm 9
Female, n (%)	188 (39%)	1528 (37%)
Race		
White	368 (76%)	3084 (75%)
Black	86 (18%)	728 (18%)
Other	32 (7%)	270 (7%)
Treatment group		
High dose vitamin	240 (49%)	2056 (50%)
Low dose vitamin	246 (51%)	2054 (50%)
Country, n (%)		
US	337 (69%)	3000 (73%)
Canada	57 (12%)	498 (12%)
Brazil	92 (19%)	612 (15%)
Graft vintage, median [IQR]	3.86 [1.70, 7.05]	4.03 [1.67, 7.46]
Living donor kidney, n (%)	207 (43%)	1705 (42%)
CVD, n (%)	93 (19%)	820 (20%)
Diabetes, n (%)	178 (37%)	1663 (41%)
Smoking, n (%)		
Never	242 (50%)	2001 (49%)
Current	57 (12%)	451 (11%)
Ever	187 (39%)	1611 (39%)
Body mass index (kg/m ²) \pm SD	29.0 \pm 5.9	29.2 \pm 6.2
SBP (mmHg) \pm SD	136 \pm 20.0	136 \pm 20
DBP (mmHg) \pm SD	79 \pm 13	78 \pm 12
eGFR (ml/min/1.73m ²) \pm SD	46 \pm 18	49 \pm 18
Urine ACR (mg/g), median [IQR]	24.5 [9.5, 105.6]	24.5 [8.72, 102.1]

Table S2. Baseline Characteristics by Quartile of Urine MCP-1 in Kidney Transplant Recipients in FAVORIT*

	Overall	Q1	Q2	Q3	Q4
Range (pg/mL)		< 84.2	84.2 - 183.3	183.4 - 351.4	≥351.4
N	473	119	118	119	117
Age ± SD	51 ± 9	52 ± 9	50 ± 9	52 ± 9	52 ± 9
Female, n (%)	182 (39%)	54 (45%)	42 (36%)	43 (36%)	43 (37%)
Race					
White	358 (76%)	106 (88%)	81 (69%)	85 (71%)	86 (74%)
Black	83 (18%)	9 (8%)	30 (25%)	25 (21%)	19 (16%)
Other	32 (7%)	4 (3%)	7 (6%)	9 (8%)	12 (10%)
Treatment group					
High dose vitamin	232 (49%)	56 (47%)	56 (48%)	56 (47%)	64 (55%)
Low dose vitamin	241 (51%)	63 (53%)	62 (53%)	63 (53%)	53 (45%)
Country, n (%)					
US	327 (69%)	97 (82%)	77 (65%)	74 (62%)	79 (68%)
Canada	54 (11%)	13 (11%)	17 (14%)	13 (11%)	11 (9%)
Brazil	92 (20%)	9 (8%)	24 (20%)	32 (27%)	27 (23%)
Graft vintage, median [IQR]	3.86 [1.70, 7.05]	3.57 [2.00, 7.41]	4.10 [1.94, 8.21]	3.63 [1.61, 6.11]	3.77 [1.39, 6.69]
Living donor kidney, n (%)	202 (43%)	54 (45%)	54 (46%)	52 (44%)	42 (36%)
Calcineurin inhibitor use, n (%)	415 (88%)	105 (88%)	104 (88%)	105 (88%)	101 (86%)
Sirolimus use, n (%)	48 (10%)	12 (10%)	7 (6%)	12 (10%)	17 (15%)
CVD, n (%)	91 (19%)	22 (19%)	24 (20%)	21 (18%)	24 (21%)
Diabetes, n (%)	173 (37%)	47 (40%)	41 (35%)	41 (35%)	44 (38%)
Smoking, n (%)					
Never	237 (50%)	55 (46%)	65 (55%)	57 (48%)	60 (51%)
Current	56 (12%)	15 (13%)	8 (7%)	16 (13%)	17 (15%)
Ever	180 (38%)	49 (41%)	45 (38%)	46 (39%)	40 (34%)
Body mass index (kg/m ²) ± SD	29.0 ± 6.0	29.0 ± 6.0	30.2 ± 6.6	28.9 ± 5.7	28.0 ± 5.4
SBP (mmHg) ± SD	136 ± 20.0	134 ± 19	135 ± 19	137 ± 21	139 ± 21
DBP (mmHg) ± SD	79 ± 13	76 ± 12	81 ± 13	79 ± 13	81 ± 13
eGFR (ml/min/1.73m ²) ± SD	46 ± 18	46 ± 16	48 ± 20	46 ± 17	45 ± 20

Ix et al, AJKD, "Urine Fibrosis Markers and Risk of Allograft Failure in Kidney Transplant Recipients: The Folic Acid for Vascular Outcome Reduction in Transplantation (FAVORIT) Trial"

Urine ACR (mg/g), median [IQR]	24.5 [9.5, 105.6]	14.6 [6.4, 45.3]	18.8 [7.9, 78.5]	28.3 [9.9, 138.4]	43.2 [14.9, 369.3]
--------------------------------	-------------------	------------------	------------------	-------------------	--------------------

* Data show characteristics by quartiles of urine MCP-1 within the Sub-Cohort Participants in FAVORIT.

Table S3. Baseline Characteristics by Quartile of Urine PIIINP in Kidney Transplant Recipients in FAVORIT*

	Overall	Q1	Q2	Q3	Q4
Range (ug/L)		< 2.09	2.09 - 3.63	3.64 - 6.15	≥ 6.16
N	488	122	122	122	122
Age ± SD	51 ± 9	53 ± 9	51 ± 9	51 ± 9	51 ± 9
Female, n (%)	188 (39%)	57 (47%)	47 (39%)	43 (35%)	41 (34%)
Race					
White	370 (76%)	106 (87%)	89 (73%)	87 (71%)	88 (72%)
Black	86 (18%)	12 (10%)	22 (18%)	23 (19%)	29 (24%)
Other	32 (7%)	4 (3%)	11 (9%)	12 (10%)	5 (4%)
Treatment group					
High dose vitamin	242 (50%)	62 (51%)	56 (46%)	62 (51%)	62 (51%)
Low dose vitamin	246 (50%)	60 (49%)	66 (54%)	60 (49%)	60 (49%)
Country, n (%)					
US	338 (69%)	89 (73%)	82 (67%)	84 (69%)	83 (68%)
Canada	58 (12%)	22 (18%)	17 (14%)	12 (10%)	7 (6%)
Brazil	92 (19%)	11 (9%)	23 (19%)	26 (21%)	32 (26%)
Graft vintage, median [IQR]	3.83 [1.68, 7.03]	4.74 [2.08, 7.99]	4.15 [2.08, 8.06]	3.64 [1.59, 6.41]	2.74 [1.07, 6.19]
Living donor kidney, n (%)	207 (42%)	49 (40%)	55 (45%)	59 (48%)	44 (36%)
Calcineurin inhibitor use, n (%)	429 (88%)	111 (91%)	110 (90%)	104 (85%)	104 (85%)
Sirolimus use, n (%)	49 (10%)	7 (6%)	6 (5%)	16 (13%)	20 (16%)
CVD, n (%)	94 (19%)	20 (16%)	28 (23%)	24 (20%)	22 (18%)
Diabetes, n (%)	179 (37%)	41 (34%)	42 (34%)	45 (37%)	51 (42%)
Smoking, n (%)					
Never	243 (50%)	52 (43%)	62 (51%)	66 (54%)	63 (52%)
Current	58 (12%)	13 (11%)	13 (11%)	15 (12%)	17 (14%)
Ever	187 (38%)	57 (47%)	47 (39%)	41 (34%)	42 (34%)
Body mass index (kg/m ²) ± SD	29.0 ± 6.0	28.7 ± 5.4	28.4 ± 5.4	29.3 ± 6.5	29.6 ± 6.4
SBP (mmHg) ± SD	136 ± 20	132 ± 18	134 ± 19	138 ± 19	140 ± 22
DBP (mmHg) ± SD	79 ± 13	76 ± 11	79 ± 12	81 ± 12	81 ± 14

Ix et al, AJKD, "Urine Fibrosis Markers and Risk of Allograft Failure in Kidney Transplant Recipients: The Folic Acid for Vascular Outcome Reduction in Transplantation (FAVORIT) Trial"

eGFR (ml/min/1.73m ²) ± SD	46 ± 18	45 ± 17	49 ± 20	47 ± 19	43 ± 15
Urine ACR (mg/g), median [IQR]	24.5 [9.5, 104.7]	16.3 [6.9, 41.1]	18.5 [7.9, 69.3]	32.1 [10.7, 141.3]	40.4 [11.9, 181.5]

* Data show characteristics by quartiles of urine PIIINP within the Sub-Cohort Participants in FAVORIT.

Table S4. Baseline Characteristics by Quartile of Urine PINP in Kidney Transplant Recipients in FAVORIT*

	Overall	Q1	Q2	Q3	Q4
Range (ug/L)		< 1.25	1.25 - 2.36	2.37 - 3.83	≥ 3.84
N	488	123	121	122	122
Age ± SD	51 ± 9	53 ± 9	51 ± 9	51 ± 9	50 ± 9
Female, n (%)	189 (39%)	51 (42%)	52 (43%)	40 (33%)	46 (38%)
Race					
White	370 (76%)	98 (80%)	101 (84%)	82 (67%)	89 (73%)
Black	86 (18%)	16 (13%)	17 (14%)	31 (25%)	22 (18%)
Other	32 (7%)	9 (7%)	3 (3%)	9 (7%)	11 (9%)
Treatment group					
High dose vitamin	242 (50%)	57 (46%)	62 (51%)	59 (48%)	64 (52%)
Low dose vitamin	246 (50%)	66 (54%)	59 (49%)	63 (52%)	58 (48%)
Country, n (%)					
US	338 (69%)	102 (83%)	80 (86%)	70 (57%)	86 (71%)
Canada	58 (12%)	10 (8%)	23 (19%)	14 (12%)	11 (9%)
Brazil	92 (19%)	11 (9%)	18 (15%)	38 (31%)	25 (21%)
Graft vintage, median [IQR]	3.86 [1.70, 7.05]	3.52 [1.61, 7.11]	4.28 [2.07, 7.33]	3.98 [2.05, 8.01]	2.92 [1.01, 6.35]
Living donor kidney, n (%)	207 (42%)	60 (49%)	50 (41%)	51 (42%)	46 (38%)
Calcineurin inhibitor use, n (%)	429 (88%)	107 (87%)	113 (93%)	108 (89%)	101 (83%)
Sirolimus use, n (%)	49 (10%)	12 (10%)	6 (5%)	10 (8%)	21 (17%)
CVD, n (%)	94 (19%)	33 (27%)	20 (17%)	20 (16%)	21 (17%)
Diabetes, n (%)	179 (37%)	51 (42%)	41 (34%)	39 (32%)	48 (39%)
Smoking, n (%)					
Never	243 (50%)	61 (50%)	56 (46%)	62 (51%)	64 (53%)
Current	58 (12%)	9 (7%)	17 (14%)	17 (14%)	15 (12%)
Ever	187 (38%)	53 (43%)	48 (40%)	43 (35%)	43 (35%)
Body mass index (kg/m ²) ± SD	29.0 ± 6.0	28.7 ± 5.9	29.4 ± 5.3	29.1 ± 6.5	28.7 ± 6.1
SBP (mmHg) ± SD	136 ± 20.0	134 ± 19	134 ± 18	138 ± 20	137 ± 23
DBP (mmHg) ± SD	79 ± 13	78 ± 10	79 ± 12	81 ± 14	79 ± 14

Ix et al, AJKD, "Urine Fibrosis Markers and Risk of Allograft Failure in Kidney Transplant Recipients: The Folic Acid for Vascular Outcome Reduction in Transplantation (FAVORIT) Trial"

eGFR (ml/min/1.73m ²) ± SD	46 ± 18	46 ± 16	47 ± 19	49 ± 18	42 ± 18
Urine ACR(mg/g), median [IQR]	24.5 [9.5, 105.6]	17.5 [7.1, 63.5]	18.1 [8.8, 54.4]	23.1 [10.2, 153.4]	46.4 [11.9, 244.7]

* Data show characteristics by quartiles of Urine PINP within the Sub-Cohort Participants in FAVORIT.

Table S5. Association of Urine Fibrosis Markers Indexed to Creatinine with Risk of Kidney Allograft Failure in FAVORIT

Range	# Events	Event Rate (per 100 PY)	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)	Model 4 HR (95% CI)
Urine α1 Microglobulin/Cr						
Per Log ₂ Increase			2.24 (1.90, 2.64); p<0.001	1.89 (1.58, 2.66); p<0.001	1.98 (1.52, 2.58); p<0.001	1.92 (1.46, 2.54); p<0.001
Q1 < 0.01	29	0.77	Reference	Reference	Reference	Reference
Q2 0.01 - 0.02	39	2.36	2.64 (1.25, 5.56)	2.12 (0.99, 4.54)	2.44 (1.10, 5.41)	2.19 (0.98, 4.87)
Q3 0.03 - 0.04	72	2.58	7.00 (3.45, 14.19)	3.90 (1.85, 8.19)	4.50 (1.98, 10.20)	4.64 (2.00, 10.77)
Q4 \geq 0.05	115	5.49	14.86 (7.15, 30.88)	7.59 (3.64, 15.81)	9.37 (3.56, 24.70)	8.57 (3.16, 23.22)
Urine MCP-1/Cr						
Per Log ₂ Increase			2.10 (1.71, 2.57); p<0.001	1.74 (1.42, 2.14); p<0.001	1.86 (1.48, 2.33); p<0.001	1.60 (1.26, 2.03); p<0.001
Q1 < 1.07	41	1.83	Reference	Reference	Reference	Reference
Q2 1.07 - 1.79	48	1.25	1.84 (0.99, 3.42)	1.97 (1.03, 3.77)	1.69 (0.85, 3.37)	1.57 (0.79, 3.14)
Q3 1.80 - 2.95	60	2.22	2.03 (1.10, 3.85)	1.35 (0.67, 2.69)	1.24 (0.58, 2.65)	1.33 (0.64, 2.78)
Q4 \geq 2.96	104	5.90	5.35 (2.89, 9.89)	3.70 (1.94, 7.06)	3.17 (1.54, 6.51)	2.37 (1.14, 4.94)
Urine PIIINP/Cr						
Per Log ₂ Increase			1.38 (1.17, 1.63); p<0.001	1.20 (1.02, 1.40); p=0.028	1.02 (0.86, 1.21); p=0.840	0.80 (0.68, 0.95); p=0.012
Q1 < 0.03	46	1.34	Reference	Reference	Reference	Reference
Q2 0.03 - 0.04	57	1.78	1.75 (0.98, 3.14)	1.29 (0.71, 2.35)	1.36 (0.73, 2.52)	0.94 (0.49, 1.80)
Q3 0.05 - 0.06	66	3.54	2.84 (1.53, 5.26)	2.08 (1.13, 3.81)	1.48 (0.76, 2.87)	0.61 (0.28, 1.30)
Q4 \geq 0.07	88	4.58	3.68 (2.03, 6.66)	1.88 (1.00, 3.52)	1.14 (0.55, 2.33)	0.35 (0.15, 0.82)
Urine PINP/Cr						
Per Log ₂ Increase			1.33 (1.18, 1.51); p<0.001	1.19 (1.05, 1.35); p=0.006	1.10 (0.96, 1.27); p=0.155	1.01 (0.88, 1.16); p=0.918
Q1 < 0.02	50	1.88	Reference	Reference	Reference	Reference
Q2 0.02 - 0.03	52	1.67	1.70 (0.95, 3.03)	1.75 (0.96, 3.18)	1.80 (0.99, 3.28)	1.65 (0.89, 3.07)
Q3 0.03 - 0.04	55	1.69	1.51 (0.84, 2.69)	0.91 (0.48, 1.72)	0.71 (0.36, 1.40)	0.60 (0.30, 1.20)
Q4 \geq 0.05	100	6.11	4.19 (2.36, 7.44)	2.89 (1.59, 5.24)	2.07 (1.09, 3.92)	1.10 (0.55, 2.23)

Model 1: Adjusted for age, sex, race, country, randomized treatment, diabetes, SBP, CVD, smoking, graft vintage, living donor.

Model 2: Model 1 plus eGFR and urine albumin.

Model 3: Model 2 plus NGAL, IL-18, KIM-1, and L-FABP

Model 4: Model 3 plus urine PIIINP, PINP, α 1microglobulin, and MCP-1

Events refers to kidney allograft failure events.