Supplementary Tables

Supplemental Table 1. Urine biomarker assay information

Assays	Study	Observed Range	Observed Average	Inter-Assay CV% Average
Albumin	WIHS	315 - ≥ 60,240 ng/mL	14,422 ng/mL	10.19%
	MACS	310 - ≥ 60,240 ng/mL	15,113 ng/mL	7.15%
β2M	WIHS	0.67 - 20,249 ng/mL	1,070 ng/mL	9.09%
	MACS	2.21 - 33,797 ng/mL	1,337 ng/mL	8.77%
Cystatin C	WIHS	4.29 - 21,210 ng/mL	132.91 ng/mL	7.60%
	MACS	2.56 - 1,927 ng/mL	58.60 ng/mL	3.74%
EGF	WIHS	0.51 - 62.57 ng/mL	15.75 ng/mL	5.98%
	MACS	0.45 - 65.08 ng/mL	11.48 ng/mL	2.74%
NGAL	WIHS	1.90 - 6,072.84 ng/mL	89.51 ng/mL	4.37%
	MACS	0.85 - 294 ng/mL	20.96 ng/mL	4.05%
OPN	WIHS	16.88 - 7,130.57 ng/mL	1,191.66 ng/mL	10.46%
	MACS	24.41 - 7016 ng/mL	995 ng/mL	5.94%
UMOD	WIHS	646.15 - 27,876 ng/mL	4,109 ng/mL	2.69%
	MACS	561 - 64,524 ng/mL	7870 ng/mL	2.81%
Clusterin	WIHS	Undetectable - 1,937,752 pg/mL	225,950 pg/mL	8.98%
	MACS	200.00 - 2,086,290 pg/mL	139,900 pg/mL	
TFF3	WIHS	Undetectable - 18,458 pg/mL	532.00 pg/mL	10.45%
	MACS	Undetectable - 8,373 pg/mL	462.00 pg/mL	
IL-18	WIHS	2.90 - 1091 pg/mL	105 pg/mL	6.19%
	MACs	1.64 - 702 pg/mL	63 pg/mL	
KIM-1	WIHS	7.97 - 8216 pg/mL	1236 pg/mL	11.68%
	MACs	0.852 - 9897 pg/mL	988 pg/mL	
MCP-1	WIHS	2.84 - 2935 pg/mL	430 pg/mL	6.53%
	MACs	0.309 - 3033 pg/mL	286 pg/mL	
YKL-40	WIHS	11.5 - 381,911 pg/mL	3938 pg/mL	4.95%
	MACs	7.63 - 4917 pg/mL	791 pg/mL	
α1m	WIHS and MACS	5-80 mg/L	n/a	4.38%, 9.15%, 9.96%
Creatinine	WIHS and MACS	1.1 - 610 mg/dL	n/a	2.25%, 2.29%

Full names for each biomarker are as follows: trefoil factor 3 (TFF3), α1-microglobulin (α1m), clusterin, uromodulin (UMOD), kidney injury molecule-1 (KIM-1), β2-microglobulin (β2M), albumin-creatinine ratio (ACR), neutrophil gelatinase-associated lipocalin (NGAL), anti-chitinase-3-like protein 1 (YKL-40), monocyte chemoattractant protein-1 (MCP-1), cystatin C (CysC), osteoponin (OPN), epidermal growth factor (EGF), and interleukin-18 (IL-18).

Supplementary Table 2. Estimated changes in urine biomarker concentrations after TDF initiation

Urine Biomarker	Year 0-1		Year 1+	
	Overall Estimated % change (95%CI)	**P-value**	**Overall** Estimated % change (95%CI)	**P-value**
TFF3	77.6 (37.6, 129.1)	< 0.0001	-0.5 (-21.8, 26.5)	0.97
α1m	32.3 (12.9, 55.1)	0.0006	2.9 (-6.6, 13.3)	0.57
Clusterin	20.8 (5.6, 38.1)	0.0063	3.2 (-7.9, 15.6)	0.59
UMOD	18.9 (4.2, 35.7)	0.010	-9.7 (-19.6, 1.4)	0.08
KIM-1	12.9 (1.2, 26.0)	0.030	5.5 (-5.7, 18.1)	0.34
β2M	10.3 (-12.0, 38.3)	0.39	12.1 (-9.9, 39.6)	0.30
ACR	9.3 (-5.6, 26.6)	0.23	9.2 (-5.7, 26.6)	0.24
NGAL	8.2 (-6.3, 24.9)	0.28	3.7 (-10.5, 20.2)	0.63
YKL-40	4.8 (-10.3, 22.4)	0.55	6.7 (-8.1, 23.8)	0.39
MCP-1	2.3 (-7.7, 13.4)	0.67	3.5 (-5.4, 13.3)	0.45
CysC	0.8 (-6.5, 8.6)	0.83	5.6 (-1.4, 13.0)	0.12
OPN	-0.6 (-8.1, 7.6)	0.88	0.6 (-6.8, 8.6)	0.88
EGF	-4.1 (-9.4, 1.5)	0.15	1.1 (-5.1, 7.8)	0.73
IL-18	-15.3 (-23.1, -6.8)	0.0008	-4.6 (-13.4, 5.1)	0.33
eGFR	-10.1 (-12.8, -7.4)	<0.001	-1.3 (-3.0, 0.5)	0.15

Estimates are adjusted for urine creatinine. Full names for each biomarker are as follows: trefoil factor 3 (TFF3), α1-microglobulin (α1m), clusterin, uromodulin (UMOD), kidney injury molecule-1 (KIM-1), β2-microglobulin (β2M), albumin-creatinine ratio (ACR), neutrophil gelatinase-associated lipocalin (NGAL), anti-chitinase-3-like protein 1 (YKL-40), monocyte chemoattractant protein-1 (MCP-1), cystatin C (CysC), osteoponin (OPN), epidermal growth factor (EGF), and interleukin-18 (IL-18). eGFR = estimated glomerular filtration rate.

Supplementary Table 3. One-year changes in urine biomarker concentrations after TDF initiation, stratified by baseline HIV RNA detectable status

Urine Biomarker	**Baseline HIV RNA** Estimated % change (95%CI)		**P-value** for interaction
	Undetectable (n=56)	**Detectable** (n=138)	
TFF3	86.3 (25.0, 177.6)	58.6 (14.4, 120.0)	0.54
α1m	80.0 (32.9, 143.8)	22.1 (0.85, 47.7)	**0.03**
Clusterin	16.8 (-11.2, 53.7)	21.8 (5.6, 40.5)	0.79
UMOD	5.6 (-16.8, 34.1)	13.1 (-1.15, 29.4)	0.63
KIM-1	42.9 (20.5, 69.5)	10.4 (-1.09, 23.3)	**0.01**
β2M	83.1 (22.0, 174.7)	-10.0 (-33.1, 21.1)	**0.006**
ACR	13.8 (-7.4, 39.9)	-5.8 (-16.8, 6.7)	0.13
NGAL	5.6 (-15.9, 32.7)	7.7 (-8.4, 26.6)	0.89
YKL-40	33.0 (2.1, 73.4)	-4.8 (-20.7, 14.4)	**0.04**
MCP-1	9.0 (-5.1, 25.3)	-1.28 (-12.2, 11.0)	0.29
CysC	4.1 (-7.0, 16.7)	0.36 (-9.0, 10.7)	0.63
OPN	-4.9 (-17.4, 9.4)	-1.51 (-10.2, 8.0)	0.68
EGF	-6.3 (-13.0, 0.88)	-1.56 (-6.0, 3.1)	0.27
IL-18	19.8 (3.1, 39.2)	-26.8 (-33.5, -19.5)	**<0.001**
eGFR	-9.5 (-15.4, 3.4)	-12 (-20, 4)	0.38

Estimates are adjusted for urine creatinine. Full names for each biomarker are as follows: trefoil factor 3 (TFF3), α1-microglobulin (α1m), clusterin, uromodulin (UMOD), kidney injury molecule-1 (KIM-1), β2-microglobulin (β2M), albumin-creatinine ratio (ACR), neutrophil gelatinase-associated lipocalin (NGAL), anti-chitinase-3-like protein 1 (YKL-40), monocyte chemoattractant protein-1 (MCP-1), cystatin C (CysC), osteoponin (OPN), epidermal growth factor (EGF), and interleukin-18 (IL-18).

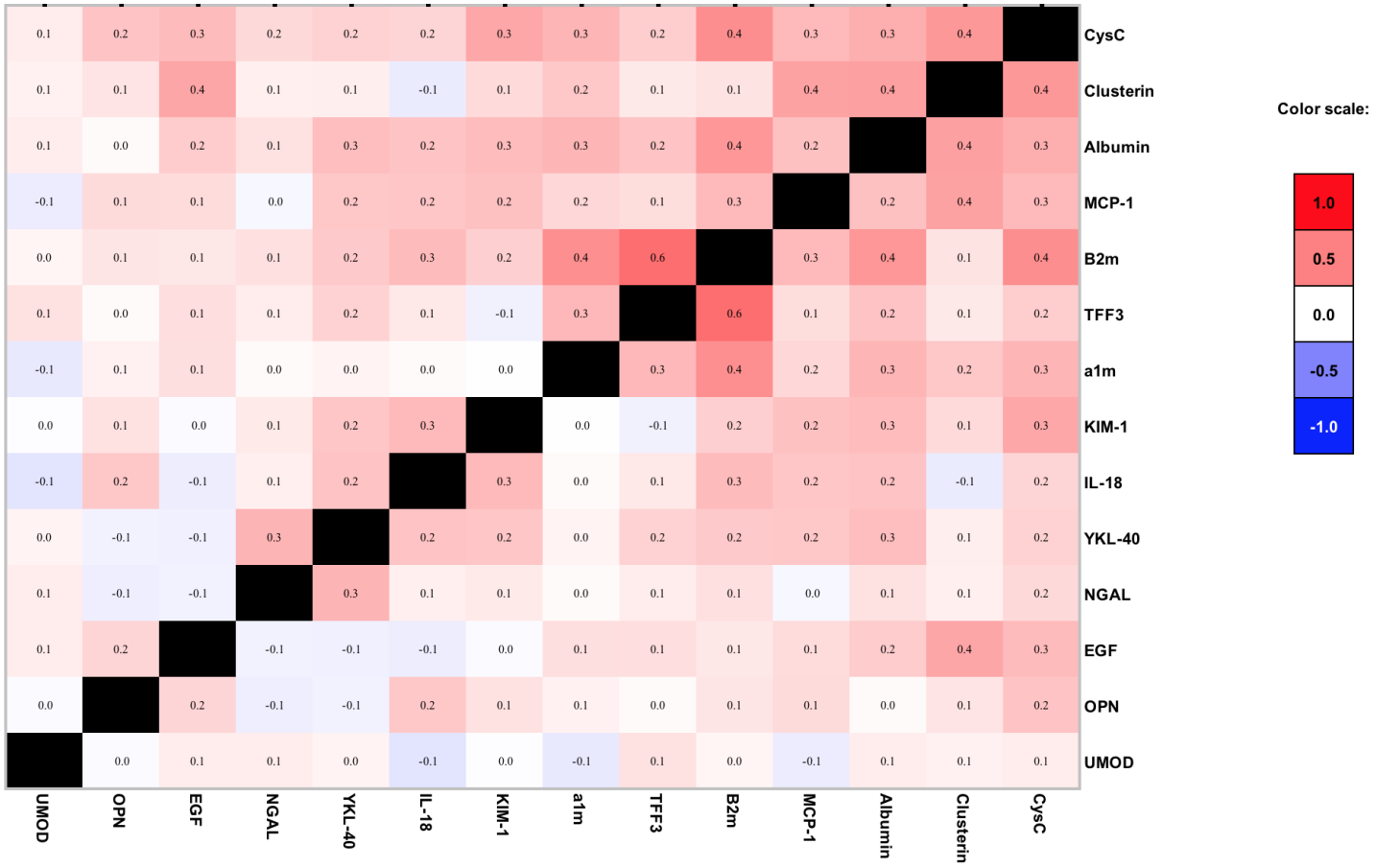
Supplementary Table 4. Estimated urine biomarker concentrations at baseline and one-year after TDF initiation, stratified by baseline HIV RNA detectable status

Biomarker	Time on TDF (years)	Baseline HIV RNA		P-value
		Undetectable (95% CI) n=56	**Detectable** (95% CI) n=138	
TFF3 (pg/mL)	0	68.0 (46.4, 99.6)	88.8 (68.4, 115.2)	0.26
	1	126.7 (81.8, 196.1)	140.8 (102.9, 192.7)	0.70
α1m (mg/dL)	0	1.03 (0.85, 1.24)	1.08 (0.96, 1.22)	0.65
	1	1.85 (1.48, 2.3)	1.32 (1.14, 1.53)	**0.01**
Clusterin (ng/mL)	0	69.6 (55.2, 87.9)	56.7 (49.9, 64.4)	0.13
	1	81.3 (62.6, 105.6)	69.1 (59.8, 79.8)	0.29
UMOD (mg/L)	0	3.6 (2.9, 4.5)	3.7 (3.3, 4.2)	0.86
	1	3.8 (3.0, 4.9)	4.2 (3.6, 4.8)	0.53
KIM-1 (pg/mL)	0	554.6 (451.3, 681.7)	601.5 (524.3, 690.1)	0.52
	1	792.6 (632.2, 993.6)	664.3 (574.0, 768.7)	0.20
β2M (ng/mL)	0	145.1 (105.9, 198.7)	289.7 (232.7, 360.6)	**<0.001**
	1	265.6 (162.0, 435.5)	260.8 (190.7, 356.6)	0.95
ACR (mg/g)	0	3.6 (2.9, 4.5)	4.7 (3.9, 5.7)	0.07
	1	4.1 (3.1, 5.4)	4.5 (3.7, 5.4)	0.62
NGAL (ng/mL)	0	15.6 (12.5, 19.6)	19.7 (16.6, 23.4)	0.11
	1	16.5 (13.3, 20.5)	21.2 (17.6, 25.6)	0.08
YKL-40 (pg/mL)	0	445.5 (346.4, 572.8)	606.5 (512.0, 718.5)	**0.047**
	1	592.6 (469.6, 747.8)	577.7 (475.2, 702.3)	0.87
MCP-1 (pg/mL)	0	201.9 (174.1, 234.2)	216.8 (194.3, 241.9)	0.45
	1	220.1 (186.2, 260.3)	214.0 (190.5, 240.5)	0.79
Cystatin C (ng/mL)	0	35.7 (31.8, 39.9)	38.2 (35.7, 41.0)	0.30
	1	37.1 (32.8, 42.1)	38.4 (35.1, 42.0)	0.67
OPN (ug/dL)	0	82.2 (73.0, 92.5)	73.0 (66.6, 80.0)	0.12
	1	78.1 (68.3, 89.4)	71.9 (65.2, 79.2)	0.32
EGF (ng/mL)	0	10.5 (9.2, 11.9)	9.4 (8.7, 10.2)	0.19
	1	9.8 (8.4, 11.4)	9.3 (8.5, 10.1)	0.56
IL-18 (pg/mL)	0	41.4 (35.6, 48.3)	72.3 (64.8, 80.6)	**<0.001**
	1	49.7 (43.1, 57.2)	52.9 (47.5, 58.9)	0.49

Marginal mean concentrations were calculated from separate linear mixed models, controlling for baseline viral load status (HIV RNA detectable vs. undetectable), time on TDF (using linear spline with cutpoint at year 1), interaction by baseline viral load, and urine creatinine. Full names for each biomarker are as follows: trefoil factor 3 (TFF3), α1-microglobulin (α1m), clusterin, uromodulin (UMOD), kidney injury molecule-1 (KIM-1), β2-microglobulin (β2M), albumin-creatinine ratio (ACR), neutrophil gelatinase-associated lipocalin (NGAL), anti-chitinase-3-like protein 1 (YKL-40), monocyte chemoattractant protein-1 (MCP-1), cystatin C (CysC), osteoponin (OPN), epidermal growth factor (EGF), and interleukin-18 (IL-18).

Supplementary Figures

Supplementary Figure 1. Heatmap of Spearman correlations of first-year urinary biomarker changes, adjusted for urine creatinine



Spearman correlations are displayed as a heat map for ease of interpretation. Positive correlations are depicted in red, and negative correlations are depicted in blue. Full names for each biomarker are as follows: trefoil factor 3 (TFF3), α1-microglobulin (α1m), clusterin, uromodulin (UMOD), kidney injury molecule-1 (KIM-1), β2-microglobulin (β2M), albumin-creatinine ratio (ACR), neutrophil gelatinase-associated lipocalin (NGAL), anti-chitinase-3-like protein 1 (YKL-40), monocyte chemoattractant protein-1 (MCP-1), cystatin C (CysC), osteoponin (OPN), epidermal growth factor (EGF), and interleukin-18 (IL-18).