Table 1S: Characteristics of Biomarker Laboratory Assays

Laboratory Assay	Manufacturer	Range	Sensitivity	Interassay CV (upper value)	Interassay CV (lower value)
Presage ST2 Assay	Critical Diagnostics, San Diego, CA	3.12 - 200 ng/ml	2.4 ng/ml	2.4% at 159.1 ng/ml	6.5% at 16.9 ng/ml
Quantikine Human GDF-15 Immunoassay	R&D Systems, Minneapolis, MN	23.4 - 1,500 pg/ml	4.39 pg/ml	5.6% at 900 pg/ml	6.0% at 225 pg/ml
Advia Centaur TnI-Ultra Assay	Siemens Medical Solutions Diagnostics, Tarrytown, NY	0.006 - 50 ng/ml	0.006 ng/ml	1.9% at 27.2 ng/ml	5.1% at 0.08 ng/ml
Roche E Modular NT-ProBNP Assay	Roche Diagnostics Corporation, Indianapolis, IN	10 - 25,000 pg/ml	1 pg/ml	1.3% at 5449 pg/ml	2.0% at 248.9 pg/ml
Quantikine Human Cystatin C Immunoassay	R&D Systems, Minneapolis, MN	3.12 - 100 ng/ml	0.227 ng/ml	5.9% at 60.9 ng/ml	7.0% at 17.2 ng/ml
Quantikine Human IL-6 Immunoassay	R&D Systems, Minneapolis, MN	3.12 - 300 pg/ml	0.7 pg/ml	3.8% at 191 pg/ml	6.4% at 17.2 pg/ml
CardioPhase High Sensitivity C-Reactive Protein Immunoassay	Siemens Medical Solutions Diagnostics, Tarrytown, NY	0.16 – 10 mg/L	0.05 mg/L	0.9% at 5.39 mg/L	2.9% at 0.42 mg/L
Zymutest D-Dimer ELISA	Aniara, West Chester, Ohio	2 – 2000 ng/ml	0.5 ng/ml	3.3% at 204 ng/ml	4.0% at 51 ng/ml
Abbreviations: CV, coefficient of variation					

Table 2S: Echocardiographic Measures and Study Outcomes for Treated, Virally-Suppressed HIV-Infected Participants and Controls

	HIV+ (N = 178)	**Control (N = 50)**	**P-value**
Ejection Fraction (%)	61.0 (56.0-65.0)	61.5 (59.0-67.0)	0.19
Systolic Dysfunction	7 (4%)	0	0.35
Diastolic Dysfunction	72 (42%)	14 (28%)	0.10
Stage 1	67 (93%)	14 (100%)	0.59
LV Mass Index (gm/m^2)	71.1 (71.1-73.6)	66.4 (63.0-72.6)	0.02
Pulmonary Hypertension	53 (30%)	1 (2.0%)	<0.001
PASP (mmHg)	31.0 (25.0-37.0)	22.5 (19.0-25.0)	<0.001
Mortality Rate*	7.3% (4.4%-12.1%)	4.0% (1.3%-12.3%)	0.34

Data are presented as Median (IQR) or numbers (percent).
* Mortality is reported as five-year rate (95% CI)
Abbreviations: LV, left ventricular; PASP, pulmonary artery systolic pressure; IQR, interquartile range

Table 3S: Baseline Characteristics of HIV-Infected Participants by Mortality Status

Characteristic	**Deceased (N = 38)**	**Alive (N = 294)**	**P-value**
Age (y)	51 (43-56)	48 (42-54)	0.27
Male	28 (74%)	242 (82%)	0.19
Race			0.089
Caucasian	16 (42%)	170 (58%)	
African American	19 (50%)	86 (29%)	
Latino	2 (5%)	20 (7%)	
Other	1 (3%)	18 (6%)	
Cigarette smoking			0.079
Current	19 (50%)	98 (33%)	
Past	11 (29%)	87 (30%)	
Never	8 (21%)	109 (37%)	
Coronary artery disease	2 (5%)	11 (4%)	0.65
Diabetes mellitus	5 (13%)	22 (7%)	0.21
Hypertension	14 (37%)	98 (33%)	0.72
Dyslipidemia	11 (55%)	119 (59%)	0.81
LDL cholesterol (mg/dL)	97 (63-130)	101 (77-128)	0.58
HDL cholesterol (mg/dL)	52 (45-59)	47 (38-55)	0.20
Triglycerides (mg/dL)	185 (73-252)	148 (101-258)	0.73
Total cholesterol (mg/dL)	186 (149-213)	184 (152-215)	0.83
Systolic blood pressure (mmHg)	122 (113-130)	120 (110-130)	0.16
Body mass index (kg/m^2)	24 (22-29)	25 (23-29)	0.18
Duration of HIV infection (y)	16 (13-20)	14 (9-18)	0.027
ARV use:			0.29
Current	34 (89%)	227 (77%)	
Past	1 (3%)	19 (6%)	
Never	3 (8%)	48 (16%)	
HAART use	33 (87%)	232 (79%)	0.29
HAART duration (y)*	5.0 (2.2-7.2)	5.4 (2.2-7.7)	---
NRTI use	35 (92%)	245 (83%)	0.23
NRTI duration (y)*	7.2 (1.0-9.8)	7.1 (2.4-9.8)	---
NNRTI use	16 (42%)	141 (48%)	0.61
NNRTI duration (y)*	2.4 (0.7-5.0)	3.3 (1.3-5.5)	---

PI use	32 (84%)	210 (71%)	0.12
PI duration (y)	5.1 (2.2-7.8)	5.4 (2.5-7.8)	---
Current Abacavir use	10 (26%)	89 (30%)	0.71
Current CD4 (cells/mm^3)	248 (168-477)	488 (314-708)	<0.001
Nadir CD4 (cells/mm^3)	88 (20-206)	176 (50-309)	0.020
Plasma HIV RNA (copies/ml):			0.0029
<75	16 (42%)	182 (62%)	
75-1999	6 (16%)	54 (18%)	
2000-9999	3 (8%)	26 (9%)	
>10000	13 (34%)	31 (11%)	
History of opportunistic infection	18 (47%)	75 (26%)	0.0070
Hepatitis C infection	20 (53%)	67 (23%)	<0.001

Data are presented as Median (IQR) or numbers (percent).
*Duration of ARV use among ever users.
Abbreviations: ARV, antiretroviral; IQR, interquartile range; HAART, highly active antiretroviral therapy; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

Table 4S: Correlations of Biomarkers among HIV-Infected Participants

	ST2	**NT-proBNP**	**GDF-15**	**Cystatin C**	**IL-6**	**D-dimer**	**hsTnI**	**hsCRP**
ST2	1	0.08	0.20*	0.17*	0.16*	0.06	0.04	0.12*
NT-proBNP		1	0.22*	0.32*	0.11	0.16*	-0.04	0.07
GDF-15			1	0.31*	-0.02	0.07	-0.09	0.07
Cystatin C				1	0.19*	0.20*	-0.05	0.13*
IL-6					1	0.25*	0.19*	0.35*
D-dimer						1	-0.06	0.33*
hsTnI							1	0.02
hsCRP								1
*Denotes statistical significance ($p<0.05$) of Spearman Correlations above								

Table 5S: Concentration of Biomarkers for Treated, Virally-Suppressed HIV-Infected Participants and Controls

Biomarker	HIV+ (N = 178)	Control (N = 50)	HIV+ versus Control			
			Unadjusted %Estimate	P-value	Adjusted %Estimate*	P-value
ST2 (ng/ml)	28.0 (22.7, 36.9)	29.2 (23.8, 33.0)	4.9 (-5.5, 16.5)	0.37	7.8 (-2.6, 19.2)	0.15
NT-proBNP (pg/ml)	39.5 (19.7, 100.3	17.7 (11.9, 32.2)	159.7 (94.6, 246.5)	<0.001	125.9 (70.3, 199.6)	<0.001
GDF-15 (pg/ml)	1072 (645, 1900)	336 (263, 431)	264.3 (204.7, 335.6)	<0.001	250.1 (192.5, 319.1)	<0.001
hsCRP (mg/L)	3.1 (1.1, 6.1)	1.9 (0.4, 4.5)	82.0 (21.9, 171.6)	0.003	75.1 (16.3, 163.6)	0.007
IL-6 (pg/ml)	3.1 (1.4, 5.8)	2.3 (1.4, 3.8)	23.8 (-8.9, 68.3)	0.17	19.1 (-13.8, 64.6)	0.29
Cystatin C (mg/L)	0.77 (0.64, 0.93)	0.61 (0.47, 0.64)	41.4 (27.9, 56.3)	<0.001	39.9 (26.0, 55.2)	<0.001
D-Dimer (ng/mL)	221 (144, 355)	183 (114, 265)	30.8 (9.5, 56.3)	0.003	22.5 (3.8, 44.5)	0.02
Detectable hsTnI (ng/ml)	45 (27%)	7 (14%)	92.9 (7.8, 245.2)	0.03	109.9 (1.4, 334.6)	0.04

Data are presented as Median (IQR) or Percent (95% Confidence Interval)
*Adjusted for Age, Gender and eGFR

Table 6S: Tests for Interactions between Individual Biomarkers with Viremia and Anti-retroviral Treatment Status for Study Outcomes in HIV-Infected Participants

Outcome	Detectable VL x Marker P-value	ARV Treatment x Marker P-value
Diastolic Dysfunction		
ST2	0.74	0.83
NT-proBNP	0.56	0.42
hsCRP	0.73	0.39
GDF-15	0.48	0.12
Cystatin C	0.71	0.89
IL-6	0.72	0.94
D-dimer	0.76	0.89
Detectable Troponin	0.46	0.21
Pulmonary Hypertension		
ST2	0.89	0.71
NT-proBNP	0.51	0.92
hsCRP	0.59	0.92
GDF-15	0.47	0.67
Cystatin C	0.72	0.65
IL-6	0.34	0.56
D-dimer	0.32	0.65
Detectable Troponin	0.07	0.62
All-cause mortality		
ST2	0.049	0.077
NT-proBNP	0.88	0.34
hsCRP	0.40	0.96
GDF-15	0.20	0.16
Cystatin C	0.83	0.38
IL-6	0.096	0.49
D-dimer	0.41	0.66
Detectable Troponin	0.17	0.49

Abbreviations: ARV, anti-retroviral; VL, viral load

Table 7S: Associations between Individual Biomarkers with Diastolic Dysfunction, Pulmonary Hypertension, and All-cause Mortality in Treated, Virally-Suppressed HIV-Infected Participants

Outcome	**Demographic-adjusted RR (95% CI)**	**Fully adjusted* RR (95% CI)**
Diastolic Dysfunction		
ST2	1.26 (0.80, 1.99), p=0.32	1.27 (0.78, 2.06), p=0.33
NT-proBNP	1.03 (0.92, 1.16), p=0.58	1.01 (0.88, 1.15), p=0.88
hsCRP	1.08 (0.95, 1.23), p=0.21	1.11 (0.96, 1.28), p=0.15
GDF-15	1.00 (0.84, 1.19), p=0.97	0.98 (0.82, 1.19), p=0.87
Cystatin C	1.13 (0.78, 1.63), p=0.51	0.99 (0.61, 1.61), p=0.98
IL-6	1.07 (0.93, 1.23), p=0.36	1.06 (0.91, 1.23), p=0.47
D-dimer	1.16 (0.91, 1.48), p=0.23	1.19 (0.91, 1.54), p=0.20
Detectable Troponin	1.37 (0.83, 2.27), p=0.22	1.24 (0.73, 2.12), p=0.42
Pulmonary Hypertension		
ST2	1.28 (0.79, 2.08), p=0.31	1.34 (0.78, 2.30), p=0.29
NT-proBNP	1.10 (0.97, 1.26), p=0.13	1.14 (0.98, 1.34), p=0.09
hsCRP	1.09 (0.95, 1.26), p=0.21	1.07 (0.92, 1.24), p=0.38
GDF-15	1.15 (0.95, 1.39), p=0.16	1.15 (0.93, 1.43), p=0.21
Cystatin C	1.28 (0.88, 1.86), p=0.19	1.39 (0.86, 2.25), p=0.18
IL-6	1.05 (0.90, 1.24), p=0.52	1.09 (0.92, 1.30), p=0.33
D-dimer	1.26 (0.95, 1.67), p=0.11	1.23 (0.90, 1.67), p=0.19
Detectable Troponin	1.01 (0.53, 1.89), p=0.99	1.26 (0.64, 2.46), p=0.51
All-cause mortality	**Demographic-adjusted HR (95% CI)**	**Fully adjusted** HR (95% CI)**
ST2	3.96 (1.52, 10.35), p=0.0050	4.12 (1.39, 12.20), p=0.011
NT-proBNP	1.30 (1.03, 1.63), p=0.028	1.20 (0.92, 1.57), p=0.18
hsCRP	1.38 (1.02, 1.87), p=0.036	1.54 (1.05, 2.25), p=0.027
GDF-15	1.95 (1.35, 2.81), p<0.001	1.89 (1.23, 2.90), p=0.0035
Cystatin C	1.81 (0.93, 3.51), p=0.079	1.33 (0.56, 3.14), p=0.52
IL-6	1.58 (1.03, 2.42), p=0.035	1.46 (0.93, 2.28), p=0.097
D-dimer	2.28 (1.26, 4.10), p=0.0061	2.05 (1.09, 3.87), p=0.027
Detectable Troponin	1.87 (0.58, 5.97), p=0.29	1.72 (0.49, 6.05), p=0.40

* For Diastolic Dysfunction and Pulmonary Hypertension, fully adjusted Poisson models control for age, gender, ethnicity, CVD risk factors (history of DM, HTN, Prior CAD, Prior MI, CHF, CKD, family history of CAD, Prior Stroke, current tobacco use, HDL, LDL), CD4 count, and HIVRNA.

**For All-cause mortality, fully adjusted Cox models control for age, gender, ethnicity, HCV, history of OI, use of aspirin or clopidogrel, and current CD4 count.

Figure 1S: Comparison of Model Discrimination for All-Cause Mortality with and without Biomarkers

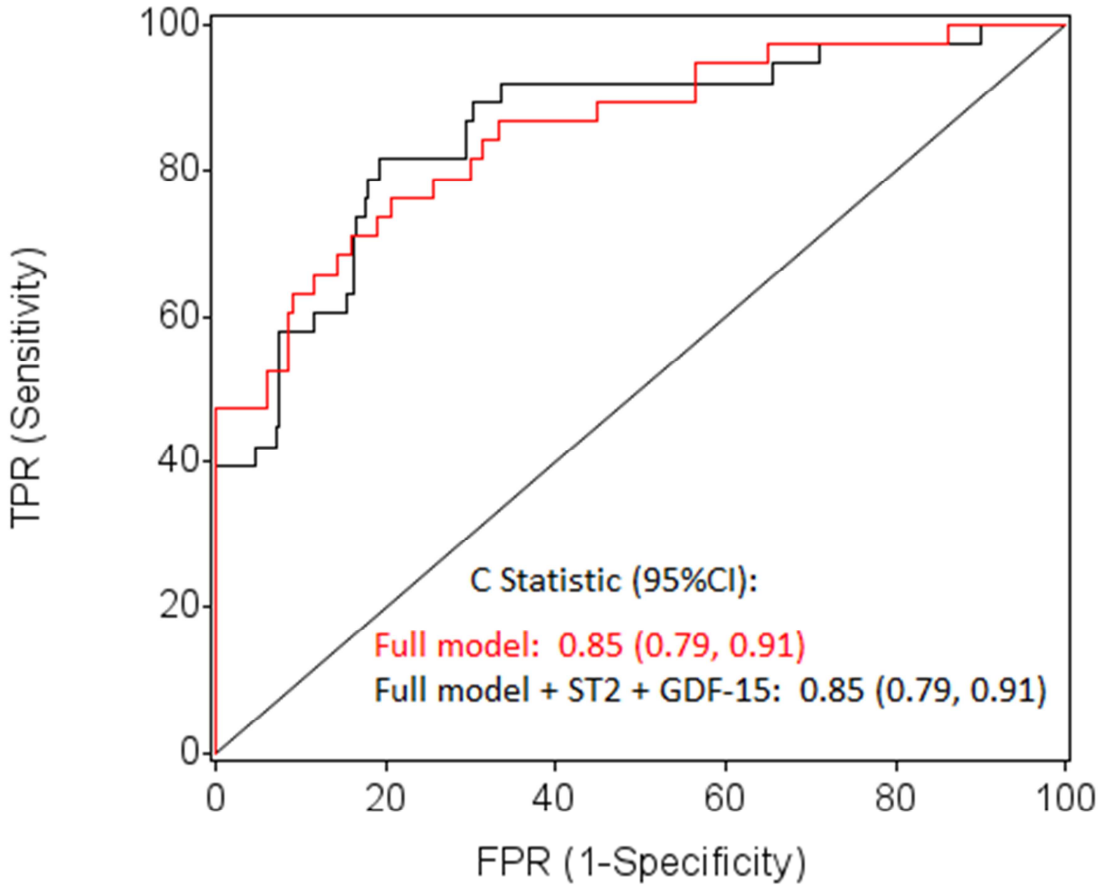

Figure Legend: Red line denotes model without biomarkers. Black line denotes model with ST2 and GDF15.
Model discrimination is assessed using Harrell's C-index of concordance for survival models. Fully adjusted Cox models control for age, gender, ethnicity, HIVRNA, HCV, history of OI, use of aspirin or clopidogrel, and current CD4 count.
FPR, false positive rate; TPR, true positive rate.