SUPPLEMENTAL MATERIAL

Table S1. Baseline patient characteristics for the biomarker cohort compared to the overall study population in SOLID-TIMI 52.

Characteristics	Overall Study Population (N=13,026)		Biomarker population (N=4,965)	
	Value	N	Value	N
Age(yrs) (median, IQR)	64 (59, 71)	13026	64 (59, 71)	4965
Age ≥60 yrs, n (%)	9661 (74.2%)	13026	3699 (74.5%)	4965
Female, n (%)	3326 (25.5%)	13026	1284 (25.9%)	4965
BMI(kg/m2) (median, IQR)	27.6 (24.8, 31.1)	12964	27.7 (25.0, 31.2)	4951
Current Smoker, n (%)	2472 (19.0%)	13014	916 (18.4%)	4961
Race (pooled)				
White, n (%)	10921 (83.8%)	13026	4364 (87.9%)	4965
Black, n (%)	315 (2.4%)	13026	129 (2.6%)	4965
Asian, n (%)	1573 (12.1%)	13026	394 (7.9%)	4965
Other, n (%)	217 (1.7%)	13026	78 (1.6%)	4965
Region (pooled)				
North America, n (%)	2806 (21.5%)	13026	1129 (22.7%)	4965
South America, n (%)	955 (7.3%)	13026	400 (8.1%)	4965
Western Europe, n (%)	3688 (28.3%)	13026	1491 (30%)	4965
Eastern Europe, n (%)	3773 (29.0%)	13026	1493 (30.1%)	4965
Asia Pacific, n (%)	1804 (13.8%)	13026	452 (9.1%)	4965
Hypertension, n (%)	9555 (73.4%)	13026	3678 (74.1%)	4965
Hyperlipidemia, n (%)	8356 (64.1%)	13024	3255 (65.6%)	4965
Diabetes Mellitus, n (%)	4502 (34.6%)	13026	1673 (33.7%)	4965
Prior MI, n (%)	4046 (31.1%)	13026	1570 (31.6%)	4965
Index Event (Pooled)				
STEMI, n (%)	5883 (45.2%)	13026	2251 (45.3%)	4965
NON-STEMI, n (%)	5559 (42.7%)	13026	2117 (42.6%)	4965
Unstable Angina, n (%)	1584 (12.2%)	13026	597 (12%)	4965
ST-Segment Deviation, n (%)	9227 (70.8%)	13019	3529 (71.1%)	4963
Activities performed for qualifying event				
Catheterization, n (%)	11201 (86.0%)	13025	4255 (85.7%)	4965
PCI, n (%)	9991 (76.7%)	13026	3774 (76%)	4965
Fibrinolytic, n (%)	1203 (9.2%)	13025	449 (9%)	4964
Days from qualifying event to randomization (median, IQR)	14 (6, 23)	13026	14 (6, 23)	4965
Baseline measurements				
eGFR (ml/min/1.73m^2) (median, IQR)	78 (66, 90)	12766	78 (66, 90)	4872
eGFR<60(mL/min/1.73m^2), n (%)	1503 (11.54%)	12766	593 (11.9%)	4872

Creatinine (mg/dL) (median IQR)	0.96 (0.81, 1.10)	12768	1 (0.8,1.1)	4874
Concomitant medical therapy				
Aspirin, n (%)	12559 (96.4%)	13021	4801 (96.7%)	4965
P2Y12 Inhibitor, n (%)	11501 (88.3%)	13021	4388 (88.4%)	4965
Statin, n (%)	12317 (94.6%)	13021	4706 (94.8%)	4965
Beta Blocker, n (%)	11364 (87.2%)	13021	4365 (87.9%)	4965
ACE or ARB, n (%)	10755 (82.6%)	13021	4125 (83.1%)	4965

IQR: interquartile range, BMI: body mass index, MI, myocardial infarction, PCI: percutaneous coronary intervention, eGFR: estimated glomerular filtration rate, ACE-I: angiotensin-converting enzyme inhibitor, ARB: angiotensin-receptor blocker

Table S2. Adjusted risk of outcomes by quartile of cystatin-C after replacing eGFR with creatinine in the main model.

Outcome	Number of events	HR & 95% CI per 1-SD of log transformed cystatin-C	*p*-value	Cystatin-C quartile				*p*-trend
				Q1 HR (95%CI)	Q2 HR (95%CI)	Q3 HR (95%CI)	Q4 HR (95%CI)	
CV Death or HF	347	1.30 (1.15-1.48)	<0.001	Referent	0.84 (0.54-1.29)	1.33 (0.90-1.97)	1.52 (1.02-2.27)	<0.01
CV death	206	1.18 (1.00-1.39)	0.06	Referent	0.84 (0.47-1.52)	1.28 (0.75-2.17)	1.3 (0.76-2.25)	0.17
Hospitalization for Heart Failure	186	1.55 (1.31-1.84)	<0.001	Referent	0.85 (0.45-1.58)	1.34 (0.76-2.35)	2.22 (1.28-3.83)	<0.01
MACE	651	1.16 (1.05-1.27)	<0.01	Referent	0.95 (0.73-1.23)	1.22 (0.95-1.56)	1.27 (0.97-1.66)	0.03
MI (fatal or non-fatal)	406	1.18 (1.04-1.33)	0.01	Referent	1.15 (0.84-1.56)	1.31 (0.97-1.78)	1.37 (0.97-1.92)	0.05
Stroke (fatal or non-fatal)	116	0.97 (0.77-1.22)	0.80	Referent	0.58 (0.30-1.11)	0.95 (0.54-1.68)	0.99 (0.541.80)	0.64
All-cause mortality	303	1.15 (1.00-1.32)	0.047	Referent	0.80 (0.52-1.23)	0.96 (0.64-1.44)	1.06 (0.70-1.59)	0.59

Variables included in the model: age (quartiles), sex, BMI (<18.5, 18.5-<25, 25-<30, ≥30), history of heart failure, diabetes mellitus, hypertension, hyperlipidemia, prior MI, current smoker, region (North America and Western Europe vs. other regions), race (white vs. non-white), index diagnosis (STEMI vs. non-STE ACS), catheterization for qualifying event, baseline LDL cholesterol (quartiles)l, days from qualifying event (≤14 days), randomized treatment arm, baseline Cys-C, baseline creatinine (<1.5 mg/dl), hsTnI (<26mg/dL), BNP (<80 pg.mL), FGF-23 (<93 pg/mL). Of note, collinearity was observed between cystatin C and creatinine when both were combined in the model although the relationship between cystatin-C and CV risk remained significant.

CV: cardiovascular, HF: heart failure, MACE: major adverse cardiovascular events, MI: myocardial infarction.

Table S3. Adjusted risk of outcomes by quartile of baseline cystatin-C, excluding FGF-23.

Outcome	HR & 95% CI per 1-SD of log transformed cystatin-C	*p*-value	Cystatin-C quartile				*p*-trend
			Q1 Adj HR (95%CI)	Q2 Adj HR (95%CI)	Q3 Adj HR (95%CI)	Q4 Adj HR (95%CI)	
CV Death or HF	1.46 (1.29-1.65)	<0.001	Referent	0.92 (0.60-1.42)	1.48 (1.00-2.18)	2.05 (1.38-3.05)	<0.001
CV death	1.43 (1.22-1.69)	<0.001	Referent	0.92 (0.51-1.65)	1.43 (0.85-2.43)	1.94 (1.13-3.32)	<0.01
Hospitalization for Heart Failure	1.60 (1.36-1.90)	<0.001	Referent	1.01 (0.55-1.86)	1.51 (0.87-2.64)	2.88 (1.67-4.97)	<0.001
MACE	1.22 (1.11-1.34)	<0.001	Referent	0.99 (0.76-1.28)	1.26 (0.98-1.61)	1.43 (1.09-1.88)	<0.01
MI (fatal or non-fatal)	1.20 (1.06-1.36)	<0.01	Referent	1.16 (0.85-1.58)	1.34 (0.99-1.81)	1.45 (1.03-2.04)	0.02
Stroke (fatal or non-fatal)	1.05 (0.83-1.32)	0.71	Referent	0.64 (0.34-1.22)	1.01 (0.57-1.79)	1.20 (0.65-2.20)	0.31
All-cause mortality	1.31 (1.14-1.50)	<0.001	Referent	0.85 (0.55-1.30)	1.06 (0.71-1.59)	1.41 (0.94-2.13)	0.06

Variables included in the model: age (quartiles), sex, BMI (<18.5, 18.5-<25, 25-<30, ≥30), history of heart failure, diabetes mellitus, hypertension, hyperlipidemia, prior MI, current smoker, region (North America and Western Europe vs. other regions), race (white vs. non-white), index diagnosis (STEMI vs. non-STE ACS), catheterization for qualifying event, baseline LDL cholesterol (quartiles)l, days from qualifying event (≤14 days), randomized treatment arm, baseline Cys-C, baseline eGFR (<60ml/min/1.73m^2), hsTnI (<26mg/dL), BNP (<80 pg/mL).

CV: cardiovascular, HF: heart failure, MACE: major adverse cardiovascular events, MI: myocardial infarction.

Table S4. Reclassification for cardiovascular death or heart failure hospitalization with Cystatin C or eGFR.

Model	Absolute IDI (95% CI)	p-value	Category-Less NRI (95% CI)	p-value
Adjusted model* + Cys-C	0.004 (0.000-0.007)	0.048	0.35 (0.25, 0.46)	<0.001
Adjusted model* + eGFR	0.001 (-0.002-0.004)	0.42	-0.16 (-0.27, -0.054)	<0.01
Adjusted model* (including eGFR) + Cys-C	0.003 (0.000-0.006)	0.07	0.28 (0.17, 0.39)	<0.001

**Variables included in the model: age (quartiles), sex, BMI (<18.5, 18.5-<25, 25-<30, ≥30), history of heart failure, diabetes mellitus, hypertension, hyperlipidemia, prior MI, current smoker, region (North America and Western Europe vs. other regions), race (white vs. non-white), index diagnosis (STEMI vs. non-STE ACS), catheterization for qualifying event, baseline LDL cholesterol (quartiles)l, days from qualifying event (≤14 days), randomized treatment arm, hsTnI (<26mg/dL), BNP (<80 pg.mL), FGF-23 (<93 pg/mL).*