

# **Supplemental Material**

**Table S1. Baseline Characteristics in Biomarker Population of SOLID – TIMI 52**

<b>Endpoint</b>	<b>Total Population</b>	<b>Biomarker Sample</b>	<b>Non-Biomarker Sample</b>	<b>P-Value</b>
	<b>No (%)</b>	<b>N (%)</b>	<b>N (%)</b>	
	<b>N=13,026</b>	<b>N=4,939</b>	<b>N=8,087</b>	
<b>Age (yrs, median, IQR)</b>	<b>64 (59, 71)</b>	<b>64 (59, 71)</b>	<b>64 (59, 71)</b>	<b>0.39</b>
<b>BMI (kg/m<sup>2</sup>, median, IQR)</b>	<b>27.6 (24.8, 31.1)</b>	<b>27.7 (25.0, 31.2)</b>	<b>27.5 (24.8, 30.9)</b>	<b>0.002</b>
<b>Female</b>	<b>3326 (25.5)</b>	<b>1275 (25.8)</b>	<b>2051 (25.4)</b>	<b>0.56</b>
<b>Race</b>				<b>&lt;0.001</b>
<b>White</b>	<b>10921 (83.8)</b>	<b>4343 (87.9)</b>	<b>6578 (81.3)</b>	
<b>Black</b>	<b>315 (2.4)</b>	<b>126 (2.6)</b>	<b>189 (2.3)</b>	
<b>Asian</b>	<b>1573 (12.1)</b>	<b>393 (8.0)</b>	<b>1180 (14.6)</b>	
<b>Other</b>	<b>217 (1.7)</b>	<b>77 (1.6)</b>	<b>140 (1.7)</b>	
<b>Region</b>				<b>&lt;0.001</b>
<b>North America</b>	<b>2806 (21.5)</b>	<b>1119 (22.7)</b>	<b>1687 (20.9)</b>	
<b>South America</b>	<b>955 (7.3)</b>	<b>392 (7.9)</b>	<b>563 (7.0)</b>	
<b>Western Europe</b>	<b>3688 (28.3)</b>	<b>1489 (30.1)</b>	<b>2199 (27.2)</b>	
<b>Eastern Europe</b>	<b>3773 (29.0)</b>	<b>1489 (30.1)</b>	<b>2284 (28.2)</b>	
<b>Asian Pacific</b>	<b>1804 (13.8)</b>	<b>450 (9.1)</b>	<b>1354 (16.7)</b>	
<b>Hypertension</b>	<b>9555 (73.4)</b>	<b>3658 (74.1)</b>	<b>5897 (72.9)</b>	<b>0.15</b>
<b>Hyperlipidemia</b>	<b>8356 (64.1)</b>	<b>3235 (65.5)</b>	<b>5121 (63.3)</b>	<b>0.013</b>
<b>Diabetes mellitus</b>	<b>4502 (34.6)</b>	<b>1670 (33.8)</b>	<b>2832 (35.0)</b>	<b>0.16</b>
<b>Prior MI</b>	<b>4046 (31.1)</b>	<b>1555 (31.5)</b>	<b>2491 (30.8)</b>	<b>0.41</b>
<b>Prior PCI</b>	<b>3112 (23.9)</b>	<b>1165 (23.6)</b>	<b>1947 (24.1)</b>	<b>0.53</b>
<b>PAD</b>	<b>1089 (8.4)</b>	<b>438 (8.9)</b>	<b>651 (8.0)</b>	<b>0.10</b>
<b>eGFR &lt;60 ml/min/1.73 m<sup>2</sup></b>	<b>1503 (11.5)</b>	<b>586 (11.9)</b>	<b>917 (11.3)</b>	<b>0.39</b>

<b>Index Event</b>				<b>0.88</b>
<b>STEMI</b>	<b>5883 (45.2)</b>	<b>2242 (45.4)</b>	<b>3641 (45.0)</b>	
<b>NSTEMI</b>	<b>5559 (42.7)</b>	<b>2104 (42.6)</b>	<b>3455 (42.7)</b>	
<b>Unstable angina</b>	<b>1584 (12.2)</b>	<b>593 (12.0)</b>	<b>991 (12.3)</b>	
<b>Aspirin</b>	<b>12559 (96.4)</b>	<b>4775 (96.7)</b>	<b>7784 (96.3)</b>	<b>0.27</b>
<b>P2Y<sub>12</sub> Inhibitor</b>	<b>11501 (88.3)</b>	<b>4367 (88.4)</b>	<b>7134 (88.2)</b>	<b>0.80</b>
<b>Statin</b>	<b>12317 (94.6)</b>	<b>4682 (94.8)</b>	<b>7635 (94.4)</b>	<b>0.42</b>
<b>Beta Blocker</b>	<b>11364 (87.2)</b>	<b>4345 (88.0)</b>	<b>7019 (86.8)</b>	<b>0.06</b>
<b>ACEI or ARB</b>	<b>10755 (82.6)</b>	<b>4106 (83.1)</b>	<b>6649 (82.2)</b>	<b>0.21</b>

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\*continuous variables are presented as medians (IQR, interquartile range) and categorical as numbers (percentages)  
†BMI, body mass index; eGFR, estimated glomerular filtration rate in ml/min/1.73 m<sup>2</sup>; PAD, peripheral artery disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-elevation MI; NSTEMI, non-ST-elevation MI; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker

**Table S2. Association of Baseline IL-6 Quartile with Cardiovascular Endpoints after Further Adjustment for Left Ventricular Dysfunction**

Endpoint	Hazard Ratio (95% Confidence Interval)			P-Trend
	Quartile 2 (N=998)	Quartile 3 (N=1005)	Quartile 4 (N=1015)	
MACE	<b>1.20 (0.91-1.58)</b>	<b>1.34 (1.02-1.77)</b>	<b>1.52 (1.11-2.07)</b>	<b>0.006</b>
CV Death/HF	<b>1.15 (0.76-1.75)</b>	<b>1.25 (0.82-1.90)</b>	<b>1.71 (1.10-2.64)</b>	<b>0.016</b>
CV Death	<b>1.03 (0.59-1.79)</b>	<b>1.41 (0.83-2.41)</b>	<b>1.83 (1.04-3.19)</b>	<b>0.019</b>
MI	<b>1.12 (0.79-1.59)</b>	<b>1.43 (1.02-2.01)</b>	<b>1.37 (0.92-2.03)</b>	<b>0.063</b>
Stroke	<b>1.46 (0.79-2.7)</b>	<b>0.88 (0.44-1.75)</b>	<b>1.36 (0.66-2.81)</b>	<b>0.73</b>
HF Hosp	<b>1.32 (0.72-2.43)</b>	<b>1.32 (0.72-2.45)</b>	<b>1.96 (1.04-3.68)</b>	<b>0.045</b>

\*Quartile 1 as reference group by Cox Proportional Hazard analysis

†MACE, major adverse cardiovascular events including CV death, MI or stroke; CV, cardiovascular; HF, heart failure; MI, myocardial infarction; Hosp, hospitalization; Model adjusted for age, sex, smoking status, body mass index, race (white versus non-white), hypertension, diabetes mellitus, peripheral artery disease, estimated glomerular filtration rate < 60 ml/min/1.73m<sup>2</sup>, hyperlipidemia, prior myocardial infarction, percutaneous coronary intervention, index qualifying event (ST-Elevation MI versus non-STE ACS), days from qualifying event, randomized treatment arm, LDL-cholesterol, biomarkers (hsCRP, Lp-PLA2, hsTnI, and BNP), and left ventricular dysfunction at discharge

**Table S3. Adjusted Risk of Cardiovascular Endpoints by Baseline IL-6 Quartile in NSTEMI ACS Population Only**

Endpoint	Hazard Ratio (95% Confidence Interval)			P-Trend
	Quartile 2 (N=694)	Quartile 3 (N=631)	Quartile 4 (N=539)	
MACE	<b>1.11 (0.84-1.47)</b>	<b>0.95 (0.7-1.28)</b>	<b>1.2 (0.85-1.69)</b>	<b>0.49</b>
CV Death/HF	<b>1.09 (0.72-1.66)</b>	<b>0.82 (0.52-1.28)</b>	<b>1.18 (0.74-1.88)</b>	<b>0.79</b>
CV Death	<b>0.95 (0.56-1.63)</b>	<b>0.78 (0.44-1.37)</b>	<b>1.17 (0.65-2.1)</b>	<b>0.78</b>
MI	<b>1.05 (0.74-1.51)</b>	<b>1.07 (0.73-1.55)</b>	<b>1.07 (0.69-1.66)</b>	<b>0.78</b>
Stroke	<b>1.14 (0.61-2.11)</b>	<b>0.54 (0.25-1.18)</b>	<b>1.3 (0.6-2.8)</b>	<b>0.98</b>
HF Hosp	<b>1.26 (0.67-2.37)</b>	<b>1.1 (0.57-2.12)</b>	<b>1.39 (0.70-2.77)</b>	<b>0.43</b>

\* Model adjusted for age, sex, smoking status, body mass index, race (white versus non-white), hypertension, diabetes mellitus, peripheral artery disease, estimated glomerular filtration rate < 60 ml/min/1.73m<sup>2</sup>, hyperlipidemia, prior myocardial infarction, percutaneous coronary intervention, days from qualifying event, randomized treatment arm, LDL-cholesterol, hsCRP, Lp-PLA2, hsTnI, and BNP with quartile 1 used as referent group

†NSTEMI, Non-ST-elevation; ACS, acute coronary syndrome; MACE, major adverse cardiovascular events including CV death, MI or stroke; CV, cardiovascular; HF, heart failure; MI, myocardial infarction; Hosp, hospitalization

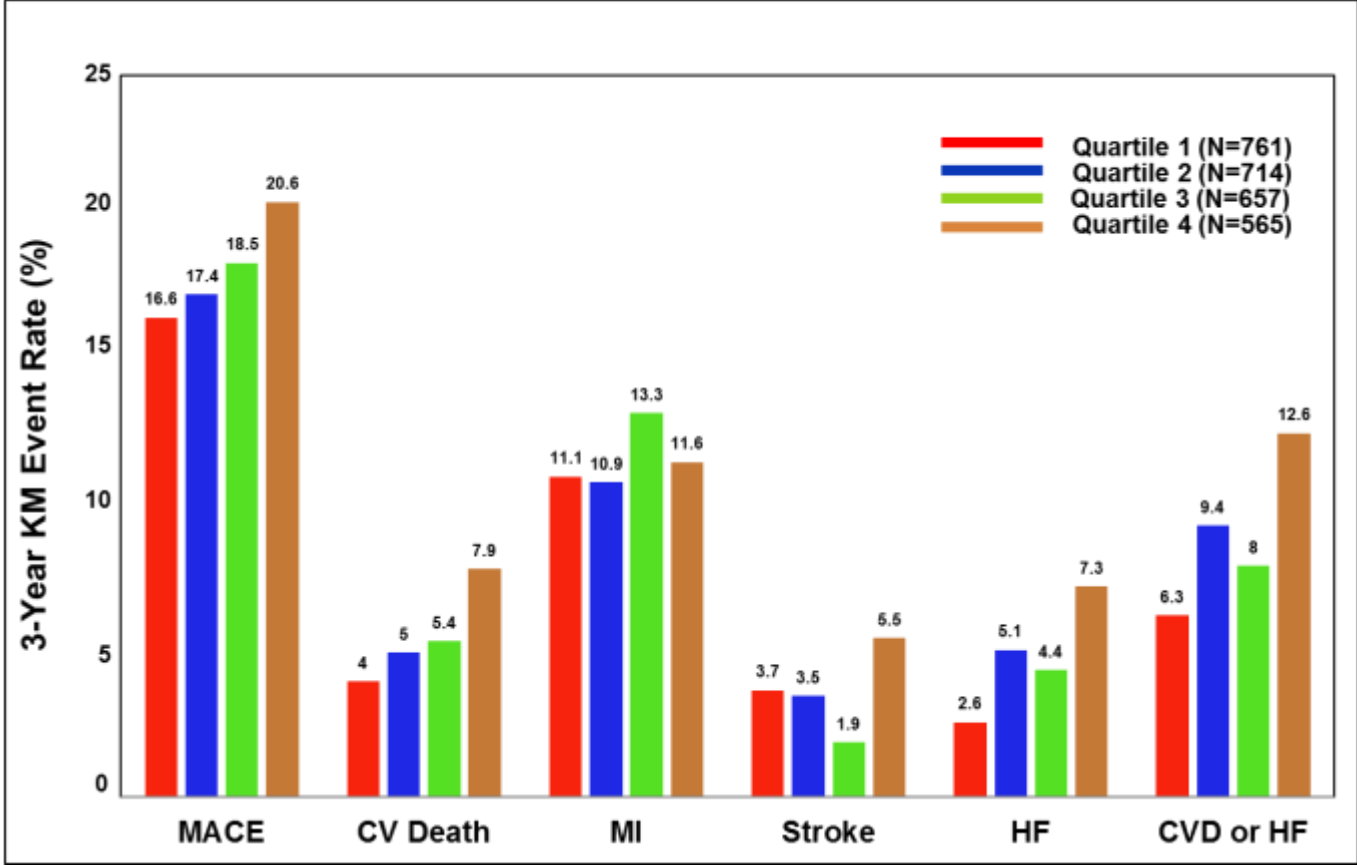
**Table S4. Adjusted Risk of Cardiovascular Endpoints by Baseline IL-6 Quartile in STEMI Population Only**

Endpoint	Hazard Ratio (95% Confidence Interval)			P-Trend
	Quartile 2 N=508	Quartile 3 N=552	Quartile 4 N=641	
MACE	1.29 (0.79-2.1)	1.86 (1.18-2.95)	1.96 (1.19-3.24)	0.003
CV Death/HF	1.80 (0.73-4.39)	3.66 (1.60-8.40)	5.33 (2.29-12.39)	<0.001
CV Death	1.19 (0.38-3.74)	3.65 (1.35-9.90)	4.63 (1.66-12.91)	<0.001
MI	1.41 (0.76-2.61)	1.85 (1.03-3.34)	1.68 (0.88-3.22)	0.08
Stroke	0.95 (0.32-2.84)	1.29 (0.46-3.67)	1.27 (0.40-4.06)	0.59
HF Hosp	2.46 (0.67-8.97)	3.13 (0.89-11.06)	5.82 (1.65-20.48)	0.005

\* Model adjusted for age, sex, smoking status, body mass index, race (white versus non-white), hypertension, diabetes mellitus, peripheral artery disease, estimated glomerular filtration rate < 60 ml/min/1.73m<sup>2</sup>, hyperlipidemia, prior myocardial infarction, percutaneous coronary intervention, days from qualifying event, randomized treatment arm, LDL-cholesterol, hsCRP, Lp-PLA2, hsTnI, and BNP with quartile 1 used as referent group

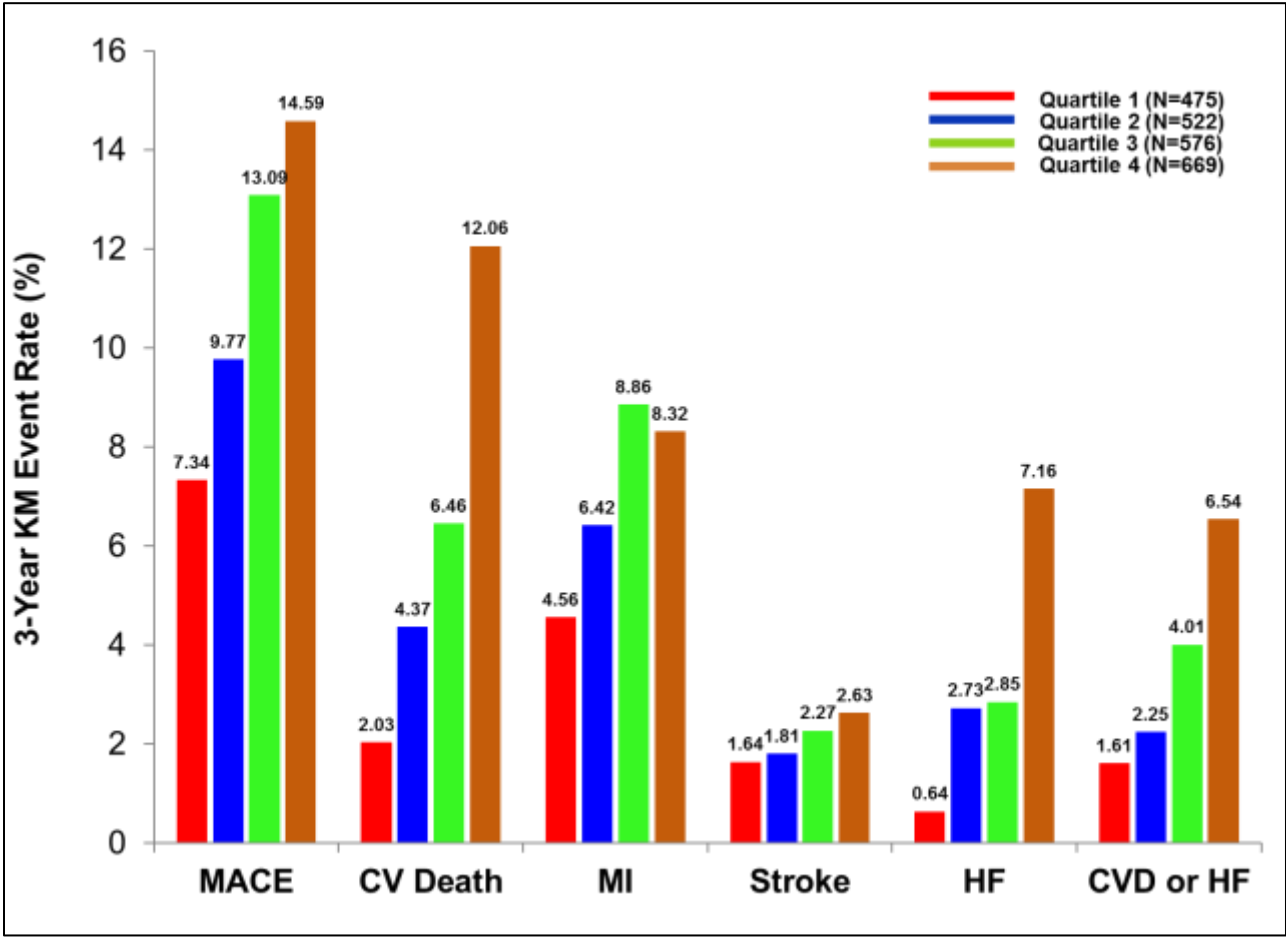
† STEMI, ST-elevation myocardial infarction; MACE, major adverse cardiovascular events including CV death, MI or stroke; CV, cardiovascular; HF, heart failure; MI, myocardial infarction; Hosp, hospitalization

**Figure S1. Unadjusted 3-Year Kaplan-Meier Event Rates of Cardiovascular Endpoints by Baseline IL-6 Quartile in NSTEMI-ACS Population Only**



NSTEMI, Non-ST-elevation; ACS, acute coronary syndrome; MACE, major adverse cardiovascular events; CV, cardiovascular; MI, myocardial infarction; HF, heart failure; CVD, cardiovascular death

**Figure S2. Unadjusted 3-Year Kaplan-Meier Event Rates of Cardiovascular Endpoints by Baseline IL-6 Quartile in STEMI Population Only**



STEMI, ST-Elevation myocardial infarction; MACE, major adverse cardiovascular events; CV, cardiovascular; MI, myocardial infarction; HF, heart failure; CVD, cardiovascular death