

**Group IIA Secretory Phospholipase A₂ and Incident Cardiovascular Disease:
An Analysis from the JUPITER Trial**

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Supplemental Material

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Supplemental Table I. Clinical characteristics of participants in the JUPITER sPLA₂-IIA cohort and overall study population

Characteristics	sPLA ₂ -IIA Cohort (N= 11,269)	Overall Cohort (N = 17,802)
Age, years	66 (60 – 71)	66 (60 – 71)
Female Sex	4187 (37)	6801 (38)
Rosuvastatin group	5624 (50)	8901 (50)
Race or ethnic group		
White	9026 (80)	12683 (71)
Black	969 (8.6)	2224 (12.5)
Asian	171 (1.5)	283 (1.6)
Hispanic	999 (8.8)	2261 (12.7)
Other or unknown	102 (1)	349 (2)
Body mass index, kg/m ²	28 (25 – 32)	28 (25 – 32)
Systolic blood pressure, mm Hg	134 (124 – 146)	134 (124 – 145)
Diastolic blood pressure, mm Hg	80 (75 – 86)	80 (75 – 87)
Current smoker	1760 (16)	2820 (16)
Family history of premature coronary disease	1398 (12)	2045 (12)
Metabolic syndrome	4351 (39)	7375 (42)
Aspirin use	1951 (17)	2958 (17)
High-sensitivity C-reactive protein, mg/L	4.2 (2.8 – 6.9)	4.3 (2.9 – 7.1)
sPLA ₂ -IIA, ng/mL	3.81 (2.49 – 6.03)	-----
low density lipoprotein -cholesterol, mg/dL	109 (94 – 119)	108 (94 – 119)
high density lipoprotein -cholesterol, mg/dL	50 (41 – 60)	49 (40 – 60)
Triglycerides, mg/dL	116 (84 – 164)	118 (85 – 169)
Total cholesterol, mg/dL	186 (170 – 200)	185 (169 – 200)
Glucose, mg/dL	94 (88 – 101)	94 (88 – 102)
Glycated hemoglobin, %	5.7 (5.4 – 5.9)	5.7 (5.5 – 5.9)
GFR, ml/min/1.73 m ² of body surface area	74 (65 – 84)	74 (65 – 84)

The values states are median (25th to 75th percentile) or n (%). Percentages may not add up because of rounding off.

sPLA₂-IIA indicates group IIA secretory phospholipases A₂;GFR, glomerular filtration rate.

Supplemental Table II. Spearman correlation coefficients of sPLA₂-IIA mass with other variables

	Baseline	On-treatment
	Spearman coefficient	Spearman coefficient
Age	0.21	0.19
Body mass index	0.09	0.11
Systolic blood pressure	0.04	-0.03
Diastolic blood pressure	-0.03	-0.07
High-sensitivity C-reactive protein	0.31	0.38
Low density lipoprotein-cholesterol	-0.04	0.05
High density lipoprotein-cholesterol	0.11	0.02
Triglycerides	-0.03	0.06
Total cholesterol	0.02	0.07
Apolipoprotein B	-0.04	0.08
Apolipoprotein A-I	0.09	-0.009
LpPLA ₂ mass	0.01	0.02
LpPLA ₂ activity	-0.17	-0.02
Glucose	-0.05	-0.04
Glycated hemoglobin	0.14	0.16
Glomerular filtration rate	-0.12	-0.16

On-treatment biomarkers were assessed at the twelve-month visit (except for glucose and glycated hemoglobin, assessed at twenty-four months) within the rosuvastatin subgroup (n=4806). sPLA₂-IIA indicates group IIA secretory phospholipases A₂; LpPLA₂, lipoprotein associated phospholipases A₂. All correlations were statistically significant (P < 0.05) except for total cholesterol and LpPLA₂ mass in the baseline; and high density lipoprotein cholesterol and apolipoprotein A-I in the on-treatment analyses.

Supplemental Table III. Median (25th to 75th percentile) concentrations of sPLA₂-IIA and hsCRP by randomized treatment group

		Baseline [*]	Year 1 [*]	Change [†]	% Change
sPLA ₂ -IIA, ng/ml	Placebo	3.8 (2.5, 6.0)	2.3 (1.4, 4.0)	-1.3 (-2.4, -0.5)	-38 (-56, -15)
	Rosuvastatin	3.9 (2.5, 6.2)	2.1 (1.3, 3.6)	-1.6 (-2.9, -0.7)	-46 (-60, -26)
hsCRP, mg/L	Placebo	4.2 (2.8, 6.9)	3.4 (1.9, 6.1)	-0.8 (-2.3, 0.8)	-20 (-50, 21)
	Rosuvastatin	4.1 (2.8, 6.8)	2.2 (1.2, 4.2)	-1.7 (-3.4, -0.6)	-48 (-69, -16)

Values obtained from individuals with both baseline and 1 year measurements (n=9 620). sPLA₂-IIA indicates group IIA secretory phospholipases A₂;hsCRP, high-sensitivity C-reactive protein. ^{*}*P* values from the Wilcoxon signed rank test comparing baseline and year 1 values were statistically significant (*P* <0.0001) [†]*P* values from the Wilcoxon rank sum test comparing the change among the rosuvastatin group with the change among the placebo group were <0.0001.

Supplementary Table IV. Incidence rates and hazard ratios with 95% confidence intervals for baseline sPLA₂-IIA mass levels and cardiovascular events among participants randomly allocated to placebo

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	<i>P</i> for trend	HR per 1-SD*	<i>P</i> -value
sPLA ₂ -IIA levels (ng/mL)	≤ 2.49	2.50 – 3.81	3.82 – 6.03	>6.03			
Primary Endpoint							
# of events / N	46/1377	45/1465	57/1431	56/1372		204/5645	
Incidence rate, per 100 person-years	1.64 (1.23-2.18)	1.48 (1.11-1.98)	1.90 (1.47-2.46)	2.01 (1.55-2.60)			
Model 1	1.00	0.93 (0.62-1.40) P=0.73	1.24 (0.83-1.83) P=0.29	1.41 (0.93-2.13) P=0.10	0.049	1.20 (1.04-1.40)	0.02
Model 2	1.00	0.89 (0.58-1.34) P=0.57	1.15 (0.77-1.72) P=0.49	1.35 (0.89-2.04) P=0.16	0.09	1.19 (1.02-1.38)	0.03
Model 3	1.00	0.88 (0.58-1.34) P=0.55	1.14 (0.76-1.71) P=0.53	1.31 (0.85-2.03) P=0.22	0.13	1.18 (1.00-1.39)	0.047
Primary Endpoint Plus Total Mortality							
# of events / N	66/ 1377	74/ 1465	93/1431	94/1372		327/5645	
Incidence rate, per 100 person-years	2.35 (1.85-2.98)	2.43 (1.94-3.05)	3.10 (2.53-3.78)	3.31 (2.72-4.04)			
Model 1	1.00	1.06 (0.76-1.48) P=0.72	1.39 (1.01-1.91) P=0.046	1.58 (1.13-2.20) P=0.007	0.002	1.26 (1.13-1.42)	<0.0001
Model 2	1.00	1.03 (0.73-1.43) P=0.88	1.30 (0.94-1.80) P=0.11	1.48 (1.06-2.07) P=0.02	0.008	1.24 (1.10-1.39)	0.0004
Model 3	1.00	1.00 (0.72-1.40) P=1.00	1.23 (0.88-1.70) P=0.22	1.30 (0.92-1.85) P=0.14	0.08	1.18 (1.03-1.36)	0.01

Model One: Adjusted for age, gender, and race.

Model Two: Adjusted for age, gender, race, smoking, family history of premature atherosclerosis, body mass index, systolic blood pressure, fasting glucose, high density lipoprotein-cholesterol, low density lipoprotein -cholesterol, and ln triglycerides

Model Three: Adjusted for age, gender, race, smoking, family history of premature atherosclerosis, body mass index, systolic blood pressure, fasting glucose, high density lipoprotein-cholesterol, low density lipoprotein -cholesterol, ln triglycerides, ln high-sensitivity C-reactive protein. sPLA₂-IIA indicates group IIA secretory phospholipases A2; HR, hazard ratio; SD, standard deviation; CVD, cardiovascular disease. $P_{\text{Interaction}}$ by randomization treatment assignment were >0.05.*Hazard ratios are expressed per 1-SD increment in ln sPLA₂-IIA

Supplementary Table V. Incidence rates and hazard ratios with 95% confidence intervals for baseline sPLA₂-IIA mass levels and cardiovascular events among participants randomly allocated to rosuvastatin

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	<i>P</i> for trend	HR per 1-SD*	<i>P</i> -value
sPLA ₂ -IIA levels (ng/mL)	≤ 2.49	2.50 – 3.81	3.82 – 6.03	>6.03			
Primary Endpoint							
# of events / N	24/1446	24/1350	25/1396	36/1432		109/5624	
Incidence rate, per 100 person-years	0.81 (0.54-1.21)	0.85 (0.57-1.27)	0.85 (0.57-1.25)	1.25 (0.90-1.73)			
Model 1	1.00	1.09 (0.62-1.93) P=0.76	1.14 (0.64-2.01) P=0.66	1.74 (1.01-3.00) P=0.047	0.05	1.23 (1.002-1.51)	0.048
Model 2	1.00	1.18 (0.66-2.11) P=0.59	1.21 (0.67-2.16) P=0.53	1.88 (1.07-3.31) P=0.03	0.03	1.26 (1.02-1.55)	0.03
Model 3	1.00	1.14 (0.64-2.05) P=0.65	1.13 (0.63-2.04) P=0.67	1.63 (0.91-2.92) P=0.10	0.11	1.17 (0.94-1.46)	0.15
Primary Endpoint Plus Total Mortality							
# of events / N	48/1446	43/1350	47/1396	64/1432		202/5624	
Incidence rate, per 100 person-years	1.62 (1.23-2.15)	1.53 (1.13-2.05)	1.59 (1.20-2.11)	2.22 (1.74-2.83)			
Model 1	1.00	0.96 (0.64-1.45) P=0.84	1.04 (0.69-1.56) P=0.86	1.45 (0.98-2.17) P=0.07	0.06	1.25 (1.08-1.45)	0.003
Model 2	1.00	1.01 (0.67-1.54) P=0.96	1.08 (0.71-1.64) P=0.72	1.48 (0.99-2.22) P=0.06	0.05	1.25 (1.07-1.45)	0.004
Model 3	1.00	0.98 (0.64-1.49) P=0.92	1.00 (0.66-1.53) P=0.99	1.25 (0.82-1.90) P=0.30	0.30	1.16 (0.99-1.35)	0.07

Model One: Adjusted for age, gender, and race.

Model Two: Adjusted for age, gender, race, smoking, family history of premature atherosclerosis, body mass index, systolic blood pressure, fasting glucose, high density lipoprotein-cholesterol, low density lipoprotein -cholesterol, and ln triglycerides

Model Three: Adjusted for age, gender, race, smoking, family history of premature atherosclerosis, body mass index, systolic blood pressure, fasting glucose, high density lipoprotein-cholesterol, low density lipoprotein -cholesterol, ln triglycerides, ln high-sensitivity C-reactive protein. sPLA₂-IIA indicates group IIA secretory phospholipases A₂; HR, hazard ratio; SD, standard deviation; CVD, cardiovascular disease. $P_{\text{Interaction}}$ by randomization treatment assignment were >0.05.*Hazard ratios are expressed per 1-SD increment in ln sPLA₂-IIA

Supplemental Table VI. SNPs with genome-wide significance for sPLA₂-IIA mass and their association with incident CVD

Chr	Gene	SNP	BP	A1	MAF	A2	β (SE)	R2	P Value	HR (95% CI)	P Value
1	<i>PLA2G2A</i>	rs11573156*	20178733	G	0.23	C	2.31 (0.06)	0.277	5.1E-472	1.11 (0.89-1.38)	0.34
1	<i>PLA2G2A</i>	rs2307246†	20177444	T	0.23	C	2.27 (0.06)	0.261	3.2 E-441	1.12 (0.90-1.39)	0.32
1	<i>PLA2G2A</i>	rs4744	20177513	T	0.23	C	2.27 (0.06)	0.262	1.1 E-441	1.11 (0.89-1.38)	0.37
1	<i>PLA2G2E/A</i>	rs10916679	20159150	A	0.27	C	1.60 (0.06)	0.133	3.2E-210	1.11 (0.90-1.37)	0.33
1	<i>PLA2G2E/A</i>	rs6672057	20166378	T	0.46	C	1.23 (0.05)	0.103	2.7E-160	1.05 (0.87-1.27)	0.59
1	<i>PLA2G5</i>	rs17354650	20262909	T	0.28	C	1.28 (0.06)	0.100	3.5E-155	1.23 (1.00-1.50)	0.05
1	<i>PLA2G2E/A</i>	rs12023742†	20164593	A	0.38	C	-1.15 (0.05)	0.090	3.6E-138	1.06 (0.88-1.29)	0.52
1	<i>PLA2G5</i>	rs2020887	20283919	T	0.35	C	0.99 (0.05)	0.062	9.2E-95	1.13 (0.93-1.37)	0.21
1	<i>PLA2G5/2D</i>	rs4655155	20300128	T	0.41	C	0.87 (0.05)	0.052	6.4E-80	1.09 (0.91-1.32)	0.34
1	<i>PLA2G2A/E</i>	rs4655020	20167609	G	0.41	T	-0.90 (0.05)	0.052	2.5E-79	0.92 (0.76-1.12)	0.42
1	<i>PLA2G2A/E</i>	rs13375942*	20164965	C	0.26	T	-0.99 (0.06)	0.052	6.4E-79	1.08 (0.87-1.34)	0.48
1	<i>PLA2G5</i>	rs11573219	20275354	C	0.42	T	0.87 (0.05)	0.051	4.6E-78	1.15 (0.95-1.38)	0.15
1	<i>PLA2G5</i>	rs11573222	20275685	A	0.41	G	0.87 (0.05)	0.051	1.2E-77	1.15 (0.95-1.39)	0.15
1	<i>PLA2G2A</i>	rs3753827	20178474	A	0.45	C	-0.80 (0.05)	0.050	4.9E-77	1.00 (0.83-1.22)	0.96
1	<i>PLA2G2A</i>	rs12732308	20170906	C	0.25	A	-0.98 (0.06)	0.050	2.9E-76	1.05 (0.85-1.31)	0.63
1	<i>PLA2G2A/E</i>	rs818968	20151992	C	0.42	T	-0.89 (0.05)	0.050	2.0E-75	0.96 (0.79-1.16)	0.66
1	<i>PLA2G2A/E</i>	rs1796924	20154556	T	0.42	C	-0.87 (0.05)	0.049	8.4E-75	0.94 (0.78-1.14)	0.53
1	<i>PLA2G5</i>	rs11573272	20286826	G	0.40	A	0.79 (0.05)	0.041	4.4E-62	1.16 (0.96-1.40)	0.11
1	<i>PLA2G5</i>	rs11573185	20267988	C	0.46	A	-0.75 (0.05)	0.039	5.6E-59	0.90 (0.74-1.08)	0.26
1	<i>PLA2G5/2C/2D/2F</i>	rs6699362	20295686	G	0.45	T	0.65 (0.05)	0.028	3.3E-43	1.18 (0.98-1.43)	0.08
1	<i>PLA2G5</i>	rs818678*	20238917	T	0.39	C	-0.65 (0.05)	0.026	9.1E-41	0.95 (0.78-1.15)	0.58
1	<i>PLA2G5/2A/2D/2F</i>	rs617363	20252732	G	0.39	A	-0.65 (0.05)	0.026	1.1E-40	0.95 (0.78-1.16)	0.63
1	<i>PLA2G5</i>	rs656110	20269827	C	0.42	T	-0.55 (0.05)	0.021	2.4E-33	0.87 (0.72-1.05)	0.15
1	<i>PLA2G2E</i>	rs4654897*	20064023	C	0.26	T	0.65 (0.06)	0.021	6.9E-33	1.05 (0.85-1.30)	0.66
1	<i>PLA2G5</i>	rs3767227	20276642	A	0.21	G	-0.71 (0.06)	0.021	1.4E-32	0.99 (0.78-1.25)	0.91
1	<i>intergenic</i>	rs4272591	20039928	A	0.26	G	0.64 (0.06)	0.021	3.3E-32	1.02 (0.82-1.26)	0.87
1	<i>OTUD3</i>	rs3738122	20111447	G	0.28	C	0.60 (0.06)	0.020	1.6E-31	1.04 (0.84-1.28)	0.73
1	<i>PLA2G2A/E</i>	rs12408941*	20158074	A	0.12	G	-0.79 (0.08)	0.020	2.1E-31	1.02 (0.77-1.35)	0.89
1	<i>PLA2G5/2A/2D/2E</i>	rs1093661	20215090	C	0.32	A	-0.51 (0.06)	0.019	2.6E-30	0.89 (0.72-1.09)	0.25
1	<i>PLA2G2A</i>	rs11677	20174551	T	0.12	C	-0.78 (0.08)	0.019	4.7E-30	1.00 (0.75-1.33)	0.99
1	<i>PLA2G5/2A/2E</i>	rs12021819	20188642	C	0.18	A	-0.71 (0.07)	0.019	1.8E-29	1.00 (0.78-1.29)	0.97
1	<i>PLA2G2A/E</i>	rs4655010	20160506	A	0.28	C	-0.58 (0.06)	0.018	1.7E-28	0.87 (0.70-1.08)	0.19
1	<i>PLA2G2A/E</i>	rs17410800	20136488	G	0.16	A	-0.72 (0.07)	0.018	2.3E-28	1.14 (0.89-1.46)	0.29
1	<i>PLA2G5</i>	rs11573238	20279173	A	0.28	G	-0.59 (0.06)	0.017	2.1E-27	0.94 (0.76-1.17)	0.60
1	<i>PLA2G5</i>	rs11573221	20275668	D	0.28	I	-0.58 (0.06)	0.017	9.9E-27	0.94 (0.76-1.17)	0.59
1	<i>PLA2G5/2C/2D/2F</i>	rs492738*	20302448	C	0.38	A	-0.47 (0.05)	0.017	1.7E-26	1.00 (0.83-1.22)	0.96
1	<i>PLA2G5</i>	rs12405285	20260195	T	0.18	C	-0.66 (0.07)	0.016	9.9E-26	0.97 (0.76-1.25)	0.83
1	<i>PLA2G5</i>	rs11573191	20269002	A	0.18	G	-0.66 (0.07)	0.016	1.0E-25	0.96 (0.75-1.23)	0.76
1	<i>PLA2G2A/E</i>	rs12132830	20151511	A	0.11	G	-0.77 (0.08)	0.015	2.4E-24	0.94 (0.69-1.29)	0.70

1	<i>PLA2G2A/E</i>	rs1093733	20131060	T	0.13	C	-0.71 (0.08)	0.015	6.3E-24	0.86 (0.64-1.16)	0.33
1	<i>intergenic</i>	rs818971	20149117	C	0.17	A	-0.64 (0.07)	0.014	5.7E-23	0.86 (0.65-1.12)	0.25
1	<i>PLA2G5/2A/2D/2F</i>	rs12410635	20245978	G	0.28	T	-0.50 (0.06)	0.014	2.9E-22	0.94 (0.76-1.16)	0.56
1	<i>PLA2G2E</i>	rs3767218	20122364	G	0.13	T	-0.67 (0.08)	0.014	6.2E-22	0.89 (0.67-1.20)	0.45
1	<i>PLA2G2E/TMCO4/OTUD3/RNF186</i>	rs10737482	20046445	T	0.39	C	0.43 (0.05)	0.014	8.8E-22	1.11 (0.91-1.34)	0.31
1	<i>PLA2G2A/E</i>	rs1796918	20135518	C	0.17	T	-0.61 (0.07)	0.013	1.7E-21	0.85 (0.65-1.11)	0.24
1	<i>PLA2G2A/E</i>	rs7531863	20118295	T	0.24	C	-0.54 (0.06)	0.013	2.3E-21	1.01 (0.81-1.26)	0.90
1	<i>PLA2G2A/E</i>	rs818963	20156530	T	0.30	C	-0.48 (0.06)	0.012	2.0E-19	0.86 (0.70-1.06)	0.16
1	<i>PLA2G2A</i>	rs2236771	20177549	C	0.09	G	-0.80 (0.09)	0.012	1.3E-18	0.74 (0.51-1.09)	0.13
1	<i>PLA2G5</i>	rs11573260*	20282127	T	0.01	C	1.80 (0.22)	0.011	3.0E-18	0.96 (0.43-2.16)	0.92
1	<i>PLA2G2E</i>	rs3767219	20122193	T	0.10	C	0.68 (0.09)	0.011	3.0E-17	1.11 (0.82-1.50)	0.50
1	<i>PLA2G2E</i>	rs2233688*	20123317	C	0.11	T	0.63 (0.09)	0.010	8.7E-17	1.32 (1.00-1.74)	0.05
1	<i>PLA2G5</i>	rs11573298	20290794	T	0.20	G	-0.52 (0.07)	0.009	5.5E-15	0.99 (0.78-1.26)	0.95
1	<i>PLA2G2E/TMCO4/OTUD3/RNF186</i>	rs4509550	20030828	C	0.40	T	-0.31 (0.05)	0.007	2.1E-12	0.94 (0.77-1.15)	0.55
1	<i>OTUD3</i>	rs10916668	20105673	A	0.07	G	-0.63 (0.10)	0.007	8.5E-12	0.75 (0.50-1.15)	0.19
1	<i>OTUD3</i>	rs10492999	20110347	G	0.07	A	-0.63 (0.10)	0.007	8.8E-12	0.75 (0.49-1.15)	0.19
1	<i>PLA2G5/2C/2D/2F/UBXN10</i>	rs12722987*	20327807	A	0.17	C	-0.38 (0.07)	0.007	1.2E-11	0.88 (0.68-1.15)	0.36
1	<i>PLA2G5/2A/2E/OTUD3</i>	rs12568139*	20184263	G	0.07	A	-0.72 (0.11)	0.007	1.7E-11	0.88 (0.59-1.32)	0.54
1	<i>PLA2G2E</i>	rs1108974	20121296	G	0.12	A	0.53 (0.08)	0.007	1.8E-11	1.13 (0.85-1.49)	0.40
1	<i>PLA2G5</i>	rs606980	20267300	A	0.11	G	-0.55 (0.09)	0.007	2.3E-11	0.97 (0.71-1.32)	0.85
1	<i>PLA2G5/2C/2D/2F/UBXN10</i>	rs12725043	20329927	G	0.17	A	-0.37 (0.07)	0.006	4.4E-11	0.90 (0.69-1.17)	0.43
1	<i>OTUD3</i>	rs12116837	20102615	A	0.05	C	-0.73 (0.12)	0.006	8.7E-11	0.64 (0.38-1.08)	0.09
1	<i>PLA2G5/2C/2D/2F/UBXN10</i>	rs656755	20296754	A	0.17	C	-0.32 (0.07)	0.006	1.0E-09	0.94 (0.73-1.21)	0.65
1	<i>OTUD3</i>	rs17401735*	20109318	G	0.18	A	-0.37 (0.07)	0.006	1.2E-09	1.11 (0.88-1.41)	0.37
17	<i>ABCA8</i>	rs34931250*†	64391522	T	0.05	C	0.59 (0.12)	0.005	3.1E-09	0.91 (0.58-1.41)	0.67
1	<i>PLA2G2E/TMCO4/OTUD3/RNF186</i>	rs12137940	20037970	A	0.08	C	-0.52 (0.10)	0.005	4.0E-09	0.75 (0.49-1.13)	0.17
1	<i>PLA2G5/2C/2D/2F/UBXN10</i>	rs623784	20325021	C	0.25	T	-0.32 (0.06)	0.005	4.5E-09	0.89 (0.72-1.12)	0.32
1	<i>intergenic</i>	rs10917560	20057522	G	0.18	T	-0.38 (0.07)	0.005	4.1E-08	1.06 (0.83-1.35)	0.65
1	<i>PLA2G2E/TMCO4/OTUD3/RNF186</i>	rs7532822	20044471	T	0.20	C	-0.38 (0.07)	0.004	4.1E-08	1.00 (0.79-1.26)	0.97
1	<i>PLA2G2D</i>	rs17354769	20319988	C	0.07	T	-0.48 (0.11)	0.004	4.7E-08	0.91 (0.62-1.35)	0.64

sPLA₂-IIA indicates group IIA secretory phospholipases A₂; Chr, chromosome, SNP, single-nucleotide polymorphism; BP, base pair position; A1, minor (effect) allele; MAF, minor allele frequency; A2, non-effect allele; SE, standard error; HR, hazard ration; and CI, confidence interval. β s and SEs were obtained from untransformed traits adjusted for age, sex, region and subpopulation stratification measures. *P* values were obtained from inverse-quantile normalized traits adjusted for age, sex, region, and subpopulation stratification measures. HRs were adjusted for drug allocation (P for interaction by drug allocation were all >0.05)

* indicates independent SNPs based on $r^2 < 0.1$ and 1Mbp distance; † indicates SNPs showing non-redundant signals from conditional GCTA analysis

Supplemental Table VII. Association of top three *PLA2G2A* variants with cardiovascular risk factors

Characteristics	rs11573156		rs2307246		rs4744	
	β (SE)	<i>P</i> Value	β (SE)	<i>P</i> Value	β (SE)	<i>P</i> Value
BMI, kg/m ²	0.052 (0.099)	0.58	0.017 (0.099)	0.83	0.011 (0.099)	0.89
SBP, mmHg	0.070 (0.279)	0.84	0.012 (0.279)	0.99	0.049 (0.280)	0.90
LDL-Cholesterol, mg/dl	-0.347 (0.311)	0.27	-0.409 (0.312)	0.29	-0.396 (0.312)	0.30
HDL-Cholesterol, mg/dl	0.390 (0.252)	0.18	0.258 (0.253)	0.41	0.284 (0.253)	0.34
Triglycerides, mg/dl	-0.586 (1.284)	0.68	-0.090 (1.289)	0.99	-0.203 (1.290)	0.95
[†] hs-CRP, mg/L	-0.251 (0.141)	0.22	-0.211 (0.141)	0.26	-0.212 (0.141)	0.29

BMI indicates body mass index; SBP, systolic blood pressure; LDL, low density lipoprotein; hs-CRP, high-sensitivity C-reactive protein; SE, standard error. β s and SEs were obtained from untransformed traits adjusted for age, sex, region and subpopulation stratification measures, and *P* values were obtained from inverse-quantile normalized traits adjusted for age, sex, region, and subpopulation stratification measures; [†] additionally adjusted for smoking status and BMI.

Supplemental Table VIII. Comparison between key factors relating to study design, population, and results between the current JUPITER study and a prior study in EPIC-Norfolk

	JUPITER	EPIC-Norfolk*
Study Design and Patient Selection		
	Prospective evaluation nested in a completed randomized controlled trial among participants without a history of cardiovascular disease who had elevated hsCRP levels and low LDL cholesterol	Nested case-control study among apparently healthy individuals
Sample Size		
	11,269 individuals with baseline sPLA2-IIA measures (9,620 also with follow-up measures at 1-year); a total of 313 incident cardiovascular disease events occurred during follow-up	1,105 cases with fatal or nonfatal coronary arterial disease and 2209 controls (age/sex/enrollment time-matched)
Patient Demographics		
Age (median years)	66	64
Proportion female (%)	37	42
sPLA2-IIA (median ng/mL)	3.81	8.5 (controls) and 9.5 (cases)
Risk Associations		
Follow-up (median, years)	1.9	6.0
Risk Estimate	Adjusted (including for hsCRP) HR (95% CI; p-trend) = 1.43 (1.01-2.03; P linear trend = 0.03) for individuals in the highest vs lowest sPLA2 quartile	Adjusted OR (95% CI; p-trend) = 1.34 (1.02, 1.71; P linear trend = 0.03) for individuals in the highest vs lowest sPLA2 quartile.

*Boekholdt *et al. Arterioscler Thromb Vasc Biol.* 2005;25:839-846.