

SUPPLEMENTAL MATERIAL

Supplemental Table 1. Baseline lipoprotein(a) concentrations according to ethnicity

Baseline Lipoprotein(a) levels (nmol / L)				
	N	Median	25 th -75 th %	90 th %
White	7730	23	10 – 50	116
Black	853	60	34 – 100	165
Asian	138	38	18 – 60	111
Hispanic	784	24	11 – 46	101
Other/Unknown	86	32	12 – 80	138
All	9591	26	11 – 56	122

N in each group reflective of number of participants with baseline Lp(a) value available.

Supplemental Table 2. Spearman correlation coefficients of lipoprotein(a) with other variables

	Baseline	On-Statins
	Spearman coefficient	Spearman coefficient
Age	0.04	0.04
BMI	- 0.07	- 0.07
SBP	- 0.03	0.009
DBP	- 0.05	- 0.02
hsCRP	0.04	0.04
LDL-C	0.13	0.18
HDL-C	0.06	0.04
Triglycerides	- 0.08	- 0.07
Total cholesterol	0.08	0.12
Apolipoprotein B	0.08	0.18
Apolipoprotein A-I	0.03	0.03
Glucose	- 0.07	- 0.07
Glycated hemoglobin	0.003	- 0.01
GFR	- 0.04	- 0.04

On-statin biomarkers assessed at the twelve-month visit (except for glucose and glycated hemoglobin, assessed at twenty-four months). All correlations were statistically significant ($P < 0.05$) except for glycated hemoglobin in the baseline Lp(a) analysis, and SBP, DBP, Apolipoprotein A-I, glycated hemoglobin, and GFR in the on-statin analysis. 7,730 and 3,877 white participants had Lp(a) concentrations available for baseline and on-statin analyses respectively.

Supplemental Table 3. Association between baseline lipoprotein(a) and clinical outcomes among white JUPITER participants randomly allocated to placebo

	Quartile One	Quartile Two	Quartile Three	Quartile Four	P-trend	HR/SD increase	P-value
Range (nmol/L)	≤ 10	11 - 23	24 - 49	≥ 50			
Primary Endpoint							
# of events / N	26 / 974	38 / 968	23 / 974	49 / 939		136 / 3855	
Incidence rate, per 100 person years	1.20	1.71	1.05	2.27	0.04	1.56	
Model One	1.00	1.44 (0.87 - 2.37) P = 0.14	0.90 (0.51 - 1.57) P = 0.75	1.93 (1.20 - 3.10) P = 0.007	0.03	1.18 (1.00 - 1.38)	0.05
Model Two	1.00	1.45 (0.88 - 2.39) P = 0.15	0.88 (0.49 - 1.53) P = 0.61	1.94 (1.19 - 3.14) P = 0.007	0.03	1.18 (1.00 - 1.39)	0.06
Primary Endpoint Plus Total Mortality							
# of events / N	37 / 974	46 / 968	33 / 974	61 / 939		177 / 3855	
Incidence rate, per 100 person years	1.70	2.07	1.51	2.82	0.05	2.02	
Model One	1.00	1.22 (0.79 - 1.89) P = 0.36	0.90 (0.56 - 1.44) P = 0.65	1.67 (1.10 - 2.51) P = 0.01	0.04	1.18 (1.03 - 1.36)	0.02
Model Two	1.00	1.24 (0.80 - 1.91) P = 0.34	0.88 (0.55 - 1.42) P = 0.60	1.69 (1.11 - 2.56) P = 0.01	0.04	1.19 (1.03 - 1.38)	0.02

Hazard ratios are expressed per 1-SD increment in ln Lp(a), with 1-SD representing an approximately 2.5-fold increment in Lp(a).

Model One: Adjusted for age and gender.

Model Two: Adjusted for age, gender, smoking, family history of premature coronary disease, body mass index, systolic blood pressure, and on-treatment levels of fasting glucose, HDL-cholesterol, LDL-cholesterol, ln triglycerides, and ln hsCRP

Supplemental Table 4. Association between baseline lipoprotein(a) and clinical outcomes among white JUPITER participants randomly allocated to rosuvastatin

	Quartile One	Quartile Two	Quartile Three	Quartile Four	P-trend	HR/SD increase	P-value
Range (nmol/L)	≤ 10	11 – 23	24 – 49	≥ 50			
Primary Endpoint							
# of events / N	18 / 1017	12 / 916	21 / 945	23 / 997		74 / 3875	
Incidence rate, per 100 person years	0.79	0.58	0.99	1.01	0.23	0.85	
Model One	1.00	0.75 (0.36 – 1.56) P = 0.45	1.24 (0.66 – 2.33) P = 0.51	1.36 (0.74 – 2.53) P = 0.33	0.17	1.24 (0.99 – 1.54)	0.06
Model Two	1.00	0.78 (0.37 – 1.62) 0.50	1.24 (0.65 – 2.37) P = 0.51	1.24 (0.65 – 2.38) P = 0.51	0.31	1.20 (0.95 – 1.50)	0.13
Primary Endpoint Plus Total Mortality							
# of events / N	22 / 1017	17 / 916	33 / 945	34 / 997		106 / 3875	
Incidence rate, per 100 person years	0.96	0.82	1.55	1.49	0.04	1.21	
Model One	1.00	0.83 (0.44 – 1.55) P = 0.56	1.50 (0.88 – 2.57) P = 0.13	1.56 (0.92 – 2.66) P = 0.10	0.03	1.29 (1.08 – 1.55)	0.01
Model Two	1.00	0.84 (0.45 – 1.59) P = 0.60	1.49 (0.86 – 2.56) P = 0.15	1.45 (0.83 – 2.51) P = 0.19	0.07	1.25 (1.04 – 1.51)	0.02

Hazard ratios are expressed per 1-SD increment in ln Lp(a), with 1-SD representing an approximately 2.5-fold increment in Lp(a).

Model One: Adjusted for age and gender.

Model Two: Adjusted for age, gender, smoking, family history of premature coronary disease, body mass index, systolic blood pressure, and on-treatment levels of fasting glucose, HDL-cholesterol, LDL-cholesterol, ln triglycerides, and ln hsCRP

Supplemental Table 5. Association between baseline lipoprotein(a) with incident primary endpoint events stratified by baseline characteristics among white JUPITER participants

		# of events / N	HR/SD	P-Value	P-interaction
Sex	Male	164 / 5161	1.20 (1.04 - 1.40)	0.01	0.86
	Female	46 / 2569	1.17 (0.89 - 1.53)	0.27	
Treatment group	Placebo	136 / 3855	1.16 (0.99 - 1.36)	0.07	0.80
	Rosuvastatin	74 / 3875	1.21 (0.97 - 1.50)	0.09	
Current smoker	No	164 / 6622	1.17 (1.01 - 1.36)	0.03	0.90
	Yes	46 / 1108	1.15 (0.88 - 1.50)	0.32	
FH of premature CHD	No	174 / 6653	1.15 (1.00 - 1.33)	0.05	0.58
	Yes	36 / 1051	1.28 (0.93 - 1.74)	0.13	
Metabolic syndrome	No	122 / 4788	1.21 (1.03 - 1.43)	0.02	0.74
	Yes	86 / 2886	1.15 (0.93 - 1.42)	0.19	
Aspirin use	No	149 / 6269	1.16 (1.00 - 1.36)	0.06	0.77
	Yes	61 / 1461	1.20 (0.95 - 1.52)	0.13	
LDL-C	≥ Median (110 mg/dl)	109 / 3904	1.15 (0.97 - 1.38)	0.12	0.83
	< Median	101 / 3824	1.19 (0.99 - 1.45)	0.07	
hsCRP	≥ Median (4.0 mg/L)	112 / 3869	1.05 (0.88 - 1.26)	0.58	0.09
	< Median	98 / 3861	1.32 (1.10 - 1.59)	0.003	
HDL-C	≥ Median (50 mg/dl)	87 / 4015	1.27 (1.05 - 1.55)	0.01	0.39
	< Median	123 / 3714	1.13 (0.95 - 1.35)	0.16	

Analysis reflects unadjusted hazard ratios per 1-SD increment in ln Lp(a). Family history of premature coronary disease defined as diagnosis of the disease in a male first-degree relative before the age of 55 years or in a female first-degree relative before the age of 65 years.

Supplemental Table 6. Association between on-statin lipoprotein(a) and residual risk among white JUPITER participants randomly allocated to rosuvastatin

	Quartile One	Quartile Two	Quartile Three	Quartile Four	P-trend	HR/SD	P-value
Range (nmol/L)	≤ 10	11 – 23	24 – 53	≥ 54			
Primary Endpoint							
# of events / N	19 / 1068	10 / 872	22 / 984	24 / 953		75 / 3877	
Incidence rate, per 100 person years	0.79	0.52	0.98	1.10	0.13	0.86	
Model One	1.00	0.65 (0.30 – 1.39) P = 0.26	1.16 (0.63 – 2.15) P = 0.63	1.47 (0.81 – 2.69) P = 0.21	0.10	1.29 (1.03 – 1.60)	0.02
Model Two	1.00	0.63 (0.29 – 1.36) P = 0.24	1.11 (0.59 – 2.09) P = 0.75	1.19 (0.63 – 2.25) P = 0.60	0.35	1.21 (0.96 – 1.53)	0.10
Primary Endpoint Plus Total Mortality							
# of events / N	23 / 1068	17 / 872	31 / 984	35 / 953		106 / 3877	
Incidence rate, per 100 person years	0.96	0.88	1.38	1.61	0.02	1.21	
Model One	1.00	0.90 (0.48 – 1.69) P = 0.75	1.33 (0.77 – 2.28) P = 0.31	1.75 (1.03 – 2.97) P = 0.04	0.02	1.30 (1.08 – 1.56)	0.006
Model Two	1.00	0.86 (0.46 – 1.62) P = 0.64	1.24 (0.71 – 2.16) P = 0.45	1.47 (0.85 – 2.56) P = 0.17	0.09	1.23 (1.02 – 1.49)	0.03

Hazard ratios are expressed per 1-SD increment in ln Lp(a), with 1-SD representing an approximately 2.5-fold increment in Lp(a).

Model One: Adjusted for age and gender.

Model Two: Adjusted for age, gender, smoking, family history of premature coronary disease, body mass index, systolic blood pressure, glucose, and on-treatment levels of HDL-cholesterol, LDL-cholesterol, ln triglycerides, and ln hsCRP.