

SUPPLEMENTARY MATERIAL

Trials with late initiation of LDL-C lowering therapy in patients without CAD or with stable CAD						
Study	Population	Treatment	Time from index event to treatment	Primary endpoint	Results	Median FU
AFCAPS/TexCAPS	No CAD n= 6605	Lovastatin 20-40mg vs. placebo	N/A	MACE (fatal/nonfatal MI, UAP, SCD)	RR 0.63 (95% CI: 0.50 to 0.79; p<0.001)	5.2 years
JUPITER	No CAD, high CRP n = 17802	Rosuvastatin 20mg vs. placebo	N/A	MACE (MI, stroke, arterial revascularization, hospitalization for UAP, cardiovascular death)	HR 0.56 (95% CI: 0.46 to 0.69; p<0.00001)	1.9 years
Cholesterol and Recurrent Events (CARE)	Stable CAD n= 4159	Pravastatin 40mg vs. placebo	10 ± 5 months Mean ± SD	MACE (fatal coronary event, nonfatal MI)	RRR 24% (95% CI: 9% to 36%; p=0.003)	5.0 years
Scandinavian simvastatin survival study (4S)	Stable CAD n = 4444	Simvastatin 10- 40mg vs. placebo	> 6 months	Total mortality	RR 0.70 (95% CI: 0.58 to 0.85; p=0.003)	5.4 years
MRC/BHF Heart Protection Study	Stable CAD n = 20536	Simvastatin 40mg vs. placebo	Not reported	MACE (mortality, fatal/nonfatal vascular events)	RR 0.87 for any death (95% CI 0.81 to 0.94; p=0.0003) RR 0.83 for any vascular (95% CI: 0.75 to 0.91; p=<0.0001)	5.0 years
FOURIER	Stable CAD n = 27564	Evolocumab 140mg vs. placebo	3.4 (1.0 – 7.4) Median (IQR)	MACE (cardiovascular death, MI, UAP requiring hospitalization, coronary revascularization, stroke)	HR 0.85 (95% CI: 0.79 to 0.92; p<0.001)	2.2 years
Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID)	Stable CAD, prior MI n = 9014	Pravastatin 40mg vs. placebo	3 months – 3 years	Mortality from CHD	RRR 24% (95% CI: 12% to 35%; p<0.001)	6.1 years
ODYSSEY OUTCOMES	Stable CAD, prior MI n = 18924	Alirocumab 75mg vs. placebo	2.6 months (1.7 – 4.4) Median (IQR)	MACE (death from CHD, nonfatal MI, fatal or nonfatal ischemic stroke, UAP requiring hospitalization)	HR 0.85 (95% CI: 0.78 to 0.93; p<0.001)	2.8 years

Supplementary table 1 Landmark trials on the effect of LDL-C lowering therapy on cardiovascular endpoints. Table is organized by study population from no CAD – stable CAD, prior MI. Abbreviations: CAD = coronary artery disease, FU = follow-up, HR = hazard ratio, IQR = interquartile range, MI = myocardial infarction, MACE = major adverse cardiac events, RR = relative risk, RRR = relative risk reduction, SCD = sudden cardiac death, SD = standard deviation, UAP = unstable angina pectoris