

Abstract

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HDL cholesterol and residual risk of first cardiovascular events after treatment with potent statin therapy: an analysis from the JUPITER trial.

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BACKGROUND: HDL-cholesterol concentrations are inversely associated with occurrence of cardiovascular events. We addressed, using the JUPITER trial cohort, whether this association remains when LDL-cholesterol concentrations are reduced to the very low ranges with high-dose statin treatment.

METHODS: Participants in the randomised placebo-controlled JUPITER trial were adults without diabetes or previous cardiovascular disease, and had baseline concentrations of LDL cholesterol of less than 3.37 mmol/L and high-sensitivity C-reactive protein of 2 mg/L or more. Participants were randomly allocated by a computer-generated sequence to receive rosuvastatin 20 mg per day or placebo, with participants and adjudicators masked to treatment assignment. In the present analysis, we divided the participants into quartiles of HDL-cholesterol or apolipoprotein A1 and sought evidence of association between these quartiles and the JUPITER primary endpoint of first non-fatal myocardial infarction or stroke, hospitalisation for unstable angina, arterial revascularisation, or cardiovascular death. This trial is registered with ClinicalTrials.gov, number NCT00239681.

FINDINGS: For 17,802 patients in the JUPITER trial, rosuvastatin 20 mg per day reduced the incidence of the primary endpoint by 44% ($p < 0.0001$). In 8901 (50%) patients given placebo (who had a median on-treatment LDL-cholesterol concentration of 2.80 mmol/L [IQR 2.43-3.24]), HDL-cholesterol concentrations were inversely related to vascular risk both at baseline (top quartile vs bottom quartile hazard ratio [HR] 0.54, 95% CI 0.35-0.83, $p = 0.0039$) and on-treatment (0.55, 0.35-0.87, $p = 0.0047$). By contrast, among the 8900 (50%) patients given rosuvastatin 20 mg (who had a median on-treatment LDL-cholesterol concentration of 1.42 mmol/L [IQR 1.14-1.86]), no significant relationships were noted between quartiles of HDL-cholesterol concentration and vascular risk either at baseline (1.12, 0.62-2.03, $p = 0.82$) or on-treatment (1.03, 0.57-1.87, $p = 0.97$). Our analyses for apolipoprotein A1 showed an equivalent strong relation to frequency of primary outcomes in the placebo group but little association in the rosuvastatin group.

INTERPRETATION: Although measurement of HDL-cholesterol concentration is useful as part of initial cardiovascular risk assessment, HDL-cholesterol concentrations are not predictive of residual vascular risk among patients treated with potent statin therapy who attain very low concentrations of LDL cholesterol.

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