

DYSLIPIDAEMIA EVOLOCUMAB LOWERS LDL CHOLESTEROL

Familial hypercholesterolaemia is characterized by impaired lipoprotein metabolism and elevated plasma concentrations of LDL cholesterol, which is associated with an increased risk of coronary artery disease. Two separate studies were undertaken to determine whether evolocumab, a monoclonal antibody against proprotein convertase subtilisin/kexin type 9 (PCSK9), can reduce LDL-cholesterol levels in patients with heterozygous or homozygous familial hypercholesterolaemia.

Investigators in the RUTHERFORD-2 trial randomly assigned 331 patients with heterozygous familial hypercholesterolaemia to four treatment groups who received: 140 mg evolocumab fortnightly, 420 mg evolocumab monthly, placebo fortnightly, or placebo monthly. After 12 weeks, the fortnightly 140 mg evolocumab group exhibited a 59.2% reduction (95% CI 53.4–65.1; $P < 0.0001$), and the monthly evolocumab group exhibited a 61.3% reduction (95% CI 53.6–69.0; $P < 0.0001$) in mean LDL-cholesterol levels compared with their respective placebo controls. Evolocumab was well-tolerated and the rate of adverse events was similar between the evolocumab and placebo groups.

Investigators conducting the TESLA Part B trial, who evaluated the efficacy of evolocumab in 49 patients with homozygous familial hypercholesterolaemia, reported similar findings. Evolocumab treatment was associated with a 30.9% reduction (95% CI –43.9 to –18.0; $P < 0.0001$) in LDL-cholesterol levels compared with placebo after 12 weeks, and did not increase the incidence of adverse events.

In an accompanying commentary, Dr Raul Santos and Dr Gerald Watts foresee that, “if proven to be safe and efficacious in the long term ... PCSK9 monoclonal antibodies might be the best standard of care for many patients with severe forms of familial hypercholesterolaemia.”

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Original articles Raal, F. J. *et al.* Inhibition of PCSK9 with evolocumab in homozygous familial hypercholesterolaemia (TESLA Part B): a randomised, double-blind, placebo-controlled trial. *Lancet* doi:10.1016/S0140-6736(14)61374-X | Raal, F. J. *et al.* PCSK9 inhibition with evolocumab (AMG 145) in heterozygous familial hypercholesterolaemia (RUTHERFORD-2): a randomised, double-blind, placebo-controlled trial. *Lancet* doi:10.1016/S0140-6736(14)61399-4 | Santos, R. D. & Watts, G. F. Familial hypercholesterolaemia: PCSK9 inhibitors are coming. *Lancet* doi:10.1016/S0140-6736(14)61702-5