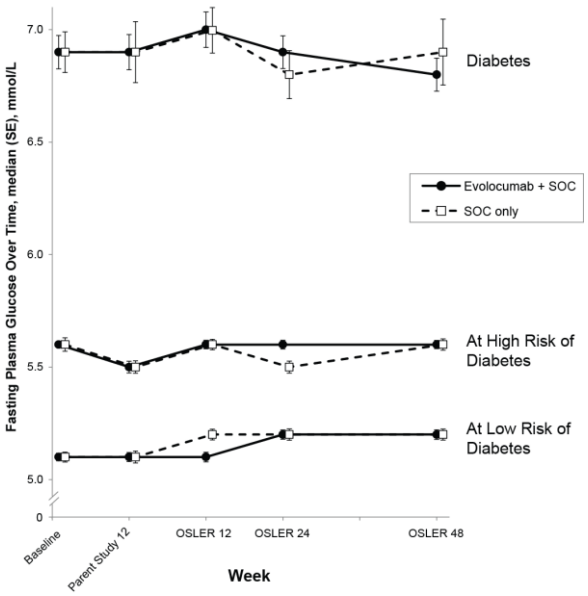
Evaluation of the one-year efficacy, safety and glycaemic effects of evolocumab (AMG 145) in 4,802 subjects with, at high risk for, or at low risk for, diabetes mellitus

N. Sattar[1], D. Preiss[1], D. Blom[2], C.S. Djedjos[3], M. Elliott[4], A. Pellacani[3], S.M. Wasserman[3], M. Koren[5], R. Holman[6];
[1]University of Glasgow, UK, [2]Division of Lipidology, Department of Medicine, University of Cape Town, South Africa, [3]Amgen Inc., Thousand Oaks, USA, [4]Amgen Limited, Cambridge, UK, [5]Jacksonville Center for Clinical Research, Jacksonville, USA, [6]Diabetes Trials Unit, OCDEM, University of Oxford, UK.

Background and aims: Statins reduce cardiovascular risk but increase the risk of developing diabetes. We investigated the effects of the PCSK9 inhibitor evolocumab (AMG 145), a fully human monoclonal antibody to PCSK9, on measures of glycaemia and adverse event (AE) rates in subjects stratified by glycaemic status.
Materials and methods: In two open-label trials (OSLER-1 and OSLER-2), 4,802 subjects completed one of 13 phase 2 or 3 parent studies of evolocumab and were randomly assigned in a 2:1 ratio to receive either evolocumab 140 mg every 2 weeks or 420 mg monthly plus standard of care (SoC) or SoC alone. SoC included statin use for some patients. Changes in fasting plasma glucose (FPG), HbA1c, and AEs were evaluated over 48 weeks in three subject groups: 852 with type 2 diabetes mellitus (T2DM), 2,432 at high risk of developing T2DM (defined as metabolic syndrome, IFG, HbA1c >6% or BMI >30kg/m2), and 1,518 at low risk of developing T2DM.
Results: LDL-C reductions for evolocumab +SoC compared with SoC were comparable across the 3 subgroups (57% to 60%). No notable differences were seen in median (SE) change in FPG from baseline to 48 weeks in patients on evolocumab + SOC compared with SoC alone (see Figure). Mean (SE) HbA1c changes at week 48 in patients on evolocumab + SoC and in patients on SoC alone were +0.16 (0.05) and +0.23 (0.06)% in patients with diabetes; +0.05 (0.01) and +0.06 (0.01)% in patients at high diabetes risk; and +0.06 (0.01) and +0.07 (0.01)% in patients at low risk of diabetes. Results were similar irrespective of parent-study drug assignment. Rates of AEs in patients on evolocumab + SoC vs. SoC alone were: 64% and 63% (T2DM); 69% and 64% (high diabetes risk); and 69% and 63% (low diabetes risk).
Conclusion: Evolocumab showed encouraging safety with no measurable effect on glycaemic parameters despite reducing LDL-C levels markedly.

Figure. Median (SE) Fasting Plasma Glucose Over Time



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