Long-term efficacy of evolocumab in reducing lipids in EU subjects with and without type 2 diabetes: An analysis from the open-label extension OSLER studies

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Background and aims: A recent meta-analysis of 12-week randomised clinical trials with the PCSK9 inhibitor evolocumab (EvoMab) in patients with hyperlipidemia showed marked reductions from baseline (BL) in lipids in subjects with (n=413) and without (n=2119) type 2 diabetes mellitus (T2DM). A 1-year pooled analysis resulted in marked reduction in lipids in subjects with and without T2DM. Here we further evaluate the long- term efficacy of EvoMab vs standard of care (SoC) on 1-year lipids level change in EU subjects with and without T2DM enrolled in the open-label extension (OLE) studies OSLER 1 and OSLER 2.

Materials and methods: A population-based 1-year interim OSLER 1 and 2 integrated analysis was performed on subjects enrolled at EU study sites. Demographic data were collected. Subjects were pooled according to the assigned OLE re-randomised 2:1 treatment (EvoMab + SoC or SoC) with the choice of 420 mg monthly or 140 mg every 2 weeks. Both EvoMab dosing regimens were combined as they have been shown to be clinically equivalent. Changes in lipids were evaluated at week 48 in subjects with and without T2DM. Results: A total of 1802 subjects were randomised from EU study sites to EvoMab + SoC or SoC, 190 with and 1612 without T2DM. T2DM subjects represented 10% of EU subjects analysis and generally presented with more cardiovascular risk factors: hypertension 83% (vs 49% all EU), coronary artery disease 34% (vs 19% all EU), and cerebrovascular/peripheral arterial disease 19% (vs 11% all EU). At week 48, reduction in lipid levels were seen in subjects with and without T2DM who received EvoMab + SoC: LDL-C (-54.1% and -48.9%), non-HDL-C (-41.6% and -40.4%), TC (-30.0% and -27.7%), Lp(a) (median % change from BL: -25.0% and -22.4%), and TG (median % change from BL: -6.8% and -3.6%). Mean increases in HDL-C were comparable in EU subjects with and without T2DM (8.2% vs 7.9%, respectively).

Conclusion: In OSLER 1 and 2 OLE EU subjects that comprised 10% of T2DM subjects, 1-year EvoMab + SoC treatment yielded significant reduction in lipid levels notably in LDL-C and Lp(a) as compared with SoC alone, with similar reductions in patients with and without T2DM. Overall, these results were consistent with previous data from 1-year pooled analysis. EvoMab as an add-on therapy to statins allows T2DM subjects to reach LDL-C treatment goals.