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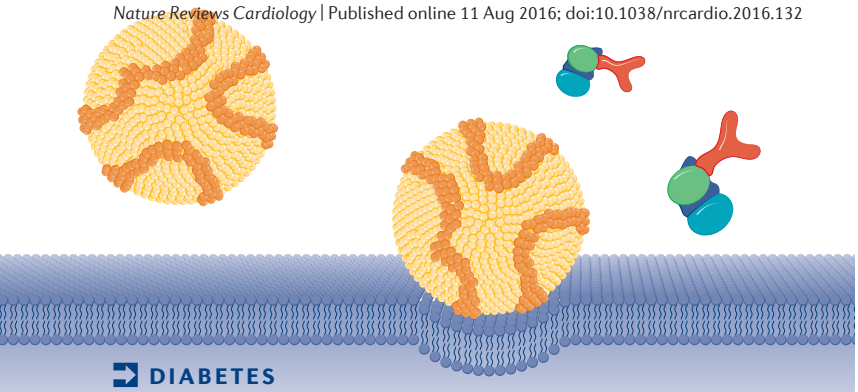

Vicky Summersby/NPG

DIABETES

# PCSK9 inhibition is not associated with new-onset diabetes

Treatment with the PCSK9 inhibitor alirocumab is not associated with transition to new-onset diabetes mellitus, according to a pooled analysis of 10 phase III clinical trials. Given the results from clinical studies showing that statin therapy modestly increases the risk of developing diabetes, and because the exact mechanisms by which statins affect glycaemic control are not yet fully understood, other therapies that lower LDL-cholesterol level, such as PCSK9 inhibitors, might also promote transition to diabetes. However, Colhoun and colleagues did not find an association between alirocumab and new-onset diabetes in the 10 ODYSSEY trials analysed. "An important aspect of our analysis is that the majority of people were already on background statin therapy," explain the investigators.

The randomized, double-blind, controlled trials included a total of 4,974 patients who were randomly assigned to receive the PSCK9 monoclonal antibody alirocumab, or either the cholesterol-lowering drug ezetimibe or placebo as comparators, with a follow-up of 6–8 months. Patients with diabetes at baseline (30.7%) were excluded from the analysis. On the basis of treatment-emergent adverse events related to diabetes, the incidence of diabetes with alirocumab was not increased compared with either placebo (HR 0.64, 95% CI 0.36–1.14) or ezetimibe (HR 0.55, 95% CI 0.22–1.41). Similarly, when both the treatment-emergent adverse events and the fasting plasma glucose and HbA1c levels were included in the analysis, alirocumab was not significantly associated with transition from pre-diabetes to new-onset diabetes compared with placebo (HR 0.90, 95% CI 0.63–1.29) or ezetimibe (HR 1.10, 95% CI 0.57–2.12).

> "This study included all available data on transition to diabetes in the ODYSSEY trials"

This study included all available data on transition to diabetes in the ODYSSEY trials. Nonetheless, the link between statin use and an increased risk of new-onset diabetes was not suggested until data from large, randomized clinical trials were available. "Longer follow-up with a larger number of individuals will be important to determine definitively the effect of PCSK9 inhibitors on the development of diabetes," caution the investigators.

*Irene Fernández-Ruiz*

**ORIGINAL ARTICLE** Colhoun, H. M. *et al.* No effect of PCSK9 inhibitor alirocumab on the incidence of diabetes in a pooled analysis from 10 ODYSSEY phase 3 studies. *Eur. Heart J.* http://dx.doi.org/10.1093/eurheartj/ehw292 (2016)
**FURTHER READING** Dadu, R. T. & Ballantyne, C. M. Lipid lowering with PCSK9 inhibitors. *Nat. Rev. Cardiol.* **11**, 563–575 (2014) | Grundy, S. M. Dyslipidaemia in 2015: Advances in treatment of dyslipidaemia. *Nat. Rev. Cardiol.* **13**, 74–75 (2016)