

IN BRIEF

DYSLIPIDAEMIA**Promising results with siRNA against PCSK9**

Two single injections of inclisiran, a small interfering RNA (siRNA) that targets PCSK9 mRNA, induce a 50% reduction in LDL-cholesterol (LDL-C) levels in 6 months, according to findings from the phase II ORION-1 trial presented at ACC.17. A total of 501 patients at high risk of cardiovascular disease and with high LDL-C levels were randomly assigned to receive one or two injections (at days 1 and 90) of inclisiran at three different doses or placebo. All inclisiran regimens induced a significant reduction in LDL-C levels at 180 days, but two injections of 300 mg inclisiran produced the greatest effect, with mean reductions from baseline of 69.1% in PCSK9 levels and 52.6% in LDL-C levels ($P < 0.001$). PCSK9 and LDL-C levels remained lower than baseline at day 240 with all doses of inclisiran.

ORIGINAL ARTICLE Ray, K. K. *et al.* Inclisiran in patients at high cardiovascular risk with elevated LDL cholesterol. *N. Engl. J. Med.* <http://dx.doi.org/10.1056/NEJMoa1615758> (2017)

DIABETES**Sacubitril/valsartan improves glycaemic control**

A *post-hoc* analysis of the PARADIGM-HF trial in a subgroup of patients with heart failure with reduced ejection fraction (HFrEF) and with known diabetes mellitus or an HbA1c level $\geq 6.5\%$ at screening shows that long-term reduction in HbA1c level is greater with sacubitril/valsartan (a dual-action angiotensin receptor–neprilysin inhibitor) than with enalapril (an angiotensin-converting enzyme inhibitor). After 1 year of treatment, HbA1c levels decreased by 0.26% in the sacubitril/valsartan group compared with a 0.16% reduction in the enalapril group ($P = 0.0023$). HbA1c levels remained lower in the sacubitril/valsartan group than in the enalapril group over 3 years of follow-up ($P = 0.0055$). New use of insulin or oral antihyperglycaemic therapy was also lower in the sacubitril/valsartan group than in the enalapril group, suggesting that sacubitril/valsartan might enhance glycaemic control in patients with HFrEF and diabetes.

ORIGINAL ARTICLE Seferovic, J. P. *et al.* Effect of sacubitril/valsartan versus enalapril on glycaemic control in patients with heart failure and diabetes: a *post-hoc* analysis from the PARADIGM-HF trial. *Lancet Diabetes Endocrinol.* [http://dx.doi.org/10.1016/S2213-8587\(17\)30087-6](http://dx.doi.org/10.1016/S2213-8587(17)30087-6) (2017)

CORONARY ARTERY DISEASE**Urbanization is a risk factor for CAD**

Results from a cross-sectional cohort study presented at ACC.17 show that Bolivian Tsimane have the lowest prevalence of coronary artery disease (CAD) of any population yet studied, with only 3% of the studied individuals having significant atherosclerotic disease, despite having a high infectious inflammatory burden. This Tsimane population had low levels of LDL cholesterol, and the presence of cardiovascular risk factors, such as obesity, hypertension, or high levels of sugar in the blood, was rare. The Tsimane live in the Bolivian Amazon and have a pre-industrial, subsistence lifestyle of hunting, gathering, fishing, and farming. The low levels of CAD in this forager–horticulturalist population suggest that urbanization and elimination of a subsistence lifestyle might be important risk factors for CAD. The authors of the study acknowledge that a subsistence diet is generally not feasible in urban populations, but adoption of some aspects of subsistence lifestyles might benefit individuals in sedentary, industrialized environments.

ORIGINAL ARTICLE Kaplan, H. *et al.* Coronary atherosclerosis in indigenous South American Tsimane: a cross-sectional cohort study. *Lancet* [http://dx.doi.org/10.1016/S0140-6736\(17\)30752-3](http://dx.doi.org/10.1016/S0140-6736(17)30752-3) (2017)