IN BRIEF

ACUTE CORONARY SYNDROMES

Targeting PCSK9 to reduce residual risk in ACS

Patients who have had an acute coronary syndrome (ACS) are at high risk of recurrent cardiovascular events, particularly patients whose LDL-cholesterol (LDL-C) levels remain elevated despite receiving high-intensity statin therapy. The ODYSSEY OUTCOMES trial now shows that treating these patients with alirocumab, a human monoclonal antibody against PCSK9, improves their cardiovascular outcomes. A total of 18,924 patients with a previous ACS who were receiving statins at high-intensity or maximum-tolerated dose were randomly assigned to receive alirocumab or placebo every 2 weeks, with the alirocumab dose adjusted to a target LDL-C level of 25–50 mg/dl. The incidence of the primary end point (a composite of death from coronary heart disease, nonfatal myocardial infarction, fatal or nonfatal ischaemic stroke or unstable angina requiring hospitalization) was lower with alirocumab than with placebo (HR 0.85, 95% CI 0.78–0.93, $P < 0.001$), with those patients with baseline LDL-C levels ≥100 mg/dl having the greatest absolute risk reduction with alirocumab therapy.

ORIGINAL ARTICLE Schwartz, G. G. et al. Alirocumab and cardiovascular outcomes after acute coronary syndrome. *N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa1801174 (2018)

CARDIOMYOPATHIES

High relapse rate after HF medication withdrawal

A pilot trial to assess the safety of withdrawing heart failure (HF) treatment in patients deemed to have recovered from dilated cardiomyopathy shows that around 40% have a relapse within 6 months of treatment withdrawal. Patients with previous dilated cardiomyopathy and clinical, imaging and biochemical evidence of recovery were randomly assigned to phased withdrawal ($n = 25$) or treatment continuation ($n = 26$). In the first 6 months, 11 patients assigned to phased withdrawal had a relapse of dilated cardiomyopathy compared with none in the continued treatment group. After 6 months, patients initially assigned to continue treatment had the treatment withdrawn, and in the following 6 months, nine patients had a relapse. According to the investigators, these findings suggest that for many patients, improved cardiac function reflects remission rather than permanent recovery, and caution that until robust variables to discriminate remission from recovery are identified, treatment should continue indefinitely.

ORIGINAL ARTICLE Halliday, B. P. et al. Withdrawal of pharmacological treatment for heart failure in patients with recovered dilated cardiomyopathy (TRED-HF): an open-label, pilot, randomised trial. *Lancet* https://doi.org/10.1016/S0140-6736(18)32484-X (2018)

DEVICE THERAPY

Feasibility of delaying coronary reperfusion

A pilot study indicates that delaying reperfusion in ST-segment elevation myocardial infarction to allow enough time for mechanical unloading of the left ventricle (LV) to precondition the myocardium and reduce injury is feasible within a short door-to-balloon time. Rates of major adverse cardiovascular and cerebrovascular events at 30 days in patients assigned to unloading of the LV with the Impella CP device (Abiomed) followed by immediate reperfusion ($n = 25$; door-to-balloon time 72 min) were similar to those in patients assigned to delayed reperfusion after 30 min of unloading ($n = 25$; door-to-balloon time 97 min) (8% versus 12%), and delaying reperfusion did not affect 30-day mean infarct size. No major safety signals were identified that would preclude a larger, pivotal trial.

ORIGINAL ARTICLE Kapur, N. K. et al. Unloading the left ventricle before reperfusion in patients with anterior ST-segment elevation myocardial infarction: a pilot study using the Impella CP®. *Circulation* https://doi.org/10.1161/CIRCULATIONAHA.118.038269 (2018)

INFLAMMATION

No benefit of methotrexate on the risk of cardiovascular events

In the CANTOS trial, anti-inflammatory therapy with canakinumab, a monoclonal antibody that selectively neutralizes IL-1β, reduced the rate of major adverse cardiovascular events in patients with stable coronary disease. By contrast, the findings of the CIRT trial, presented at the 2018 AHA Scientific Sessions by Paul Ridker, the lead investigator of both studies, showed that low-dose methotrexate, a drug used to treat inflammatory conditions such as rheumatoid arthritis, did not reduce adverse cardiovascular events in patients with stable atherosclerosis who were at high cardiovascular risk. Despite a neutral outcome, the CIRT trial provides additional information on designing future therapeutic strategies for these patients.

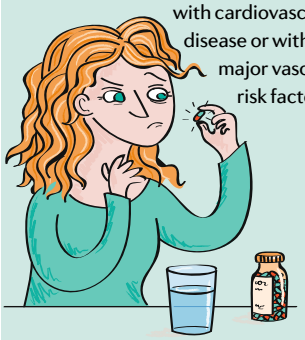
The CIRT trial was designed and ran in parallel to the CANTOS trial to determine whether a broad-spectrum anti-inflammatory agent could show similar benefits to those seen with IL-1β-targeted anti-inflammatory therapy. In the double-blind trial, 4,786 patients with previous myocardial infarction or multivessel coronary disease who additionally had either type 2 diabetes mellitus or the metabolic syndrome were randomly assigned to receive low-dose methotrexate (2,391 patients) or placebo (2,395 patients). After a median follow-up of 2.3 years, the final primary end point — a composite of nonfatal myocardial infarction, nonfatal stroke, cardiovascular death or hospitalization for unstable angina that led to urgent revascularization — occurred in 201 patients in the methotrexate group and in 207 patients in the placebo group (HR 0.96, 95% CI 0.79–1.16). No significant differences were observed between the two

PREVENTION

Dietary supplements undergo VITAL test

Intake of marine n-3 fatty acids or dietary supplementation with vitamin D_3 have limited benefits in reducing the risk of cardiovascular disease or cancer in generally healthy men and women, according to data from the VITAL trial presented at the AHA Scientific Sessions 2018.

Most of the previous trials on n-3 (also known as omega-3) fatty acids had been conducted in high-risk patients with cardiovascular disease or with major vascular risk factors, and the trials on vitamin D generally focused on bone health. "The VITAL trial was designed to fill knowledge gaps on the role of vitamin D_3 and marine n-3 fatty acid supplements in the primary prevention of cancer and cardiovascular disease in 'usual risk' populations," says JoAnn Manson, lead investigator of the trial. VITAL included 25,871 participants (aged ≥50 years) without cardiovascular disease or cancer at baseline who were randomly assigned to receive high-dose vitamin D_3 (2,000 IU per day), marine n-3 fatty acids (Omacor fish oil; 1 g per day) or placebo.



Credit: Lara Crow/Springer Nature Limited

After an average of 5.3 years, fish-oil supplementation was associated with a small but nonsignificant 8% reduction in major cardiovascular events (composite primary end point of myocardial infarction (MI), stroke and cardiovascular mortality) compared with placebo. For key secondary end points, fish-oil intake significantly reduced the incidence