IN BRIEF

ACUTE CORONARY SYNDROME

Prasugrel superior to ticagrelor in ACS

A prasugrel-based strategy is associated with a lower incidence of death, myocardial infarction (MI) or stroke than a ticagrelor-based strategy in patients with an acute coronary syndrome (ACS) with or without ST-segment elevation who are scheduled to undergo invasive evaluation. These findings come from the ISAR-REACT 5 trial, conducted in Germany and Italy, and were presented at the ESC Congress 2019. Patients assigned to ticagrelor ($n = 2{,}012$) received the loading dose as soon as possible after randomization; in the prasugrel group ($n = 2{,}006$), therapy was initiated as soon as possible after randomization in patients with ST-segment elevation but was postponed until after assessment of the coronary anatomy for those without ST-segment elevation. The rate of the primary end point (a composite of death, MI or stroke at 1 year) was 9.3% with ticagrelor and 6.9% with prasugrel (HR 1.36, 95% CI 1.09–1.70, $P = 0.006$). The lower incidence of the primary end point with prasugrel was driven by fewer MIs. The rate of major bleeding events was not significantly different between the groups.

ORIGINAL ARTICLE Schüpke, S. et al. Ticagrelor or prasugrel in patients with acute coronary syndromes. *N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa1908973 (2019)

ANTITHROMBOTIC THERAPY

Rivaroxaban monotherapy for AF and stable CAD

Monotherapy with the non-vitamin K antagonist oral anticoagulant rivaroxaban is noninferior for efficacy and superior for safety compared with combination therapy with rivaroxaban plus a single antiplatelet agent in patients with atrial fibrillation (AF) and stable coronary artery disease (CAD), according to results from the AFIRE trial presented at the ESC Congress 2019. The trial was stopped early owing to increased mortality in the combination-therapy group. The trial was conducted in Japan and included 2,236 patients with AF who had undergone revascularization >1 year earlier or who had confirmed CAD not requiring revascularization. The rate of the primary efficacy end point (a composite of cardiovascular events and all-cause death) was similar in the rivaroxaban and combination-therapy groups (HR 0.72, 95% CI 0.55–0.95, $P < 0.001$ for noninferiority). Major bleeding event rates were lower with rivaroxaban monotherapy than with combination therapy (HR 0.59, 95% CI 0.39–0.89, $P = 0.01$ for superiority).

ORIGINAL ARTICLE Yasuda, S. et al. Antithrombotic therapy for atrial fibrillation with stable coronary disease. *N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa1904143 (2019)

ANTITHROMBOTIC THERAPY

Edoxaban noninferior to VKA in AF after PCI

Dual therapy with edoxaban plus a $P2Y_{12}$ inhibitor is noninferior to triple therapy with a vitamin K antagonist (VKA) plus a $P2Y_{12}$ inhibitor and aspirin for the risk of bleeding in patients with atrial fibrillation (AF) who had undergone percutaneous coronary intervention (PCI). These results from the ENTRUST-AF PCI trial were presented at the ESC Congress 2019. The trial was conducted in 18 countries and included 1,506 patients with AF who had had a successful PCI. Median time from PCI to randomization was 45.1 h. At 1 year, major or clinically relevant nonmajor bleeding events occurred in 17% and 20% of patients in the edoxaban and VKA groups, respectively (HR 0.83, 95% CI 0.65–1.05, $P = 0.001$ for noninferiority). Both groups had similar rates of the main efficacy outcome of ischaemic events.

ORIGINAL ARTICLE Vranckx, P. et al. Edoxaban-based versus vitamin K antagonist-based antithrombotic regimen after successful coronary stenting in patients with atrial fibrillation (ENTRUST-AF PCI): a randomised, open-label, phase 3b trial. *Lancet* https://doi.org/10.1016/S0140-6736(19)31872-0 (2019)

PHARMACOGENETICS

Reduced bleeding with genotype-guided antiplatelet therapy

Genotype-guided selection of oral $P2Y_{12}$ inhibitor therapy can reduce the incidence of bleeding in patients undergoing primary percutaneous coronary intervention (PCI). This finding from the randomized, open-label POPular Genetics trial was presented at the ESC Congress 2019.

Dual antiplatelet therapy with aspirin and a $P2Y_{12}$ inhibitor is recommended after PCI with stent implantation to prevent recurrent thrombotic events. The $P2Y_{12}$ inhibitors prasugrel and ticagrelor are more potent than clopidogrel and are, therefore, preferred because of their greater efficacy; however, prasugrel and ticagrelor also increase the risk of bleeding.

Some patients have an inadequate response to clopidogrel therapy because of loss-of-function variation in *CYP2C19*, such as the *CYP2C19**2 or *CYP2C19**3 alleles, which impairs the conversion of the prodrug to its active metabolite. However, in patients without these loss-of-function alleles, clopidogrel has been shown to be as effective as prasugrel or ticagrelor, with a lower risk of bleeding. "If we treated patients with the more potent inhibitors ticagrelor and prasugrel only if their *CYP2C19* genetic profile showed that they would not metabolize clopidogrel effectively, this [approach] would benefit patient outcomes," hypothesize the POPular Genetics trial investigators.

A total of 2,488 patients undergoing PCI were randomly assigned to genotype-guided therapy or standard therapy (prasugrel or ticagrelor). Approximately two-thirds of the patients in the genotype-guided group received clopidogrel.

BIOMARKERS

AI-derived adipose tissue biomarker for risk prediction using CCTA

Inflammation in coronary vessels is characterized by changes in the composition of perivascular adipose tissue (PVAT), which can be measured by the Fat Attenuation Index (FAI) on coronary CT angiography (CCTA). However, this biomarker does not account for any structural changes in adipose tissue. In a study presented at the ESC Congress 2019 and published in the *European Heart Journal*, Antoniades and colleagues describe a novel machine-learning-derived biomarker, the fat radiomic profile (FRP), that can detect PVAT remodelling and improve cardiac risk prediction beyond traditional risk-stratification algorithms.

The FAI, developed as a surrogate of coronary inflammation, has been shown to be a powerful predictor of cardiac and all-cause mortality. "However, as FAI changes dynamically with treatments, a repeat measurement is needed when a patient starts medication that affects coronary inflammation," explains Antoniades. Given that inflammation can also induce structural changes in PVAT, his group sought to identify additional, less variable biomarkers through CCTA-based radiomic phenotyping.

The CT radiomic profile of PVAT composition was quantified using a radiotranscriptomic approach from biopsies obtained from 167 patients undergoing cardiac surgery. CT radiomic features were linked to markers of inflammation, fibrosis and vascularity. Using an artificial intelligence (AI)-powered approach, 1,391 radiomic features from 101 patients who had major adverse cardiac events (MACE) within 5 years of having a CCTA and from 101 healthy controls were used to develop an algorithm (termed the FRP) to distinguish between cases and controls. The FRP signature was