Evolocumab Improves Cardiovascular Outcomes

Statin-treated patients with atherosclerotic CVD and relatively low baseline LDL levels had significant outcomes benefits with evolocumab, beyond its further LDL-lowering effects.

Prior research on evolocumab:

- A monoclonal antibody that inhibits proprotein convertase subtilisin–kexin type 9 (PCSK9) — has shown that this now FDA-approved drug can reduce LDL-cholesterol levels by 50% to 60% (NEJM JW Cardiol Jun 2014 and N Engl J Med 2014; 370:1811). New data came from FOURIER, a manufacturer-funded outcomes trial of the drug (NCT01764633).
- Researchers randomized 27,564 statin-treated patients with atherosclerotic cardiovascular disease (CVD) and LDL levels ≥70 mg/dL (median, 92 mg/dL) to receive subcutaneous evolocumab (140 mg every 2 weeks or 420 mg every month, as the patient preferred) or matching placebo. By 48 weeks of treatment, the drug had reduced LDL levels by 59%, compared with placebo, to a median of 30 mg/dL.
- During a median follow-up of 2.2 years, incidence of the primary composite endpoint — cardiovascular death, myocardial infarction (MI), stroke, hospitalization for unstable angina, or coronary revascularization — was significantly lower with evolocumab than with placebo (9.8% vs. 11.3%; hazard ratio, 0.85; 95% confidence interval, 0.79–0.92), as was incidence of the main secondary endpoint of cardiovascular death, MI, or stroke (5.9% vs. 7.4%; HR, 0.80; 95% CI, 0.73–0.88). Findings were consistent across major subgroups. No prominent safety concerns emerged. There was no difference in all-cause mortality.

REFERENCE
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Low Iron Stores in Healthy Children Affect EKG Markers

Both an excess of iron and iron deficiency (ID) may lead to significant cardiac problems. Parameters that represent ventricular repolarization heterogeneity, like QT dispersion (QTd), corrected QT dispersion (QTcd), the interval between the peak and the end of the T wave (Tp-e), and Tp-e dispersion, have not been evaluated in otherwise healthy children with low iron levels before.

Here we assessed the effects of low iron storage on P wave dispersion (PWd), QTd, Tp-e intervals, and Tp-e dispersion in otherwise healthy children. 283 patients who were referred to pediatric cardiology department for cardiac evaluation due to murmurs and who were found to have no structural heart disease were prospectively reviewed.

The patients were divided into three groups according to their ferritin levels: Group 1: ferritin <15 ng/mL (n = 58); Group 2: ferritin 15–25 ng/mL (n = 80); Group 3: ferritin >25 ng/mL (n = 145). P wave duration (PW), QT and Tp-e intervals, and PW, QT, corrected QT (QTc), and Tp-e dispersions were significantly higher in patients whose ferritin level was <15 ng/mL. A negative correlation was found between ferritin level and QT and QTc intervals, and QT, QTc, and Tp-e dispersions.

The results showed that a low serum ferritin level is associated with changes in some ECG parameters such as prolonged PWd, Tp-e interval, QT, QTc, and Tp-e dispersions in otherwise healthy children, and studies of other populations indicated that these parameters may predict arrhythmias in selected patients. These patients may be considered at some risk of developing arrhythmias. Therefore, careful evaluation of these ECG parameters is necessary in otherwise healthy children with low iron stores.

REFERENCE
Karadeniz, C., Özdemir, R., Demirol, M. et al. Pediatr Cardiol (2017). doi:10.1007/s00246-017-1596-7.
Dual Antithrombotic vs. Dual Antiplatelet Strategy after Acute Coronary Syndrome

Replacing one antiplatelet agent with an anticoagulant did not increase bleeding risk, but neither did it show any signal of ischemic benefit. Although dual antiplatelet therapy (DAPT) with a P2Y<sub>12</sub> inhibitor (clopidogrel, prasugrel, or ticagrelor) and aspirin is the standard of care after an acute coronary syndrome (ACS), major cardiovascular events still occur after ACS in almost 10% of patients.

Adding low-dose rivaroxaban, an anticoagulant, to DAPT resulted in a decrease in ischemic outcomes but increased major bleeding events (NEJM JW Cardiology 2011 Nov 13).

To explore the effects on bleeding outcomes of replacing one antiplatelet agent with an anticoagulant, investigators conducted an industry-funded, double-blind, randomized trial (NCT02293395) of aspirin versus low-dose rivaroxaban in 3037 ACS patients who were taking a P2Y<sub>12</sub> inhibitor (mean age, 63; ST-segment elevation myocardial infarction [STEMI], 49%; non-STEMI, 40%; unstable angina, 11%). Treatment was started at a median of 5.5 days after ACS, median treatment duration was 291 days, and median follow-up was 326 days.

The rate of the primary endpoint (Thrombosis In Myocardial Infarction clinically significant bleeding not related to coronary artery bypass grafting) was 5% in both the rivaroxaban and the aspirin groups, with no significant interaction between treatment assignment and any of the subgroups examined. The rate of an exploratory ischemic endpoint (composite of cardiovascular death, MI, stroke, and definite stent thrombosis) was also 5% in both the rivaroxaban and the aspirin groups.

Comment

In this study, the risk for clinically significant bleeding did not differ between patients who received DAPT and those who received dual-pathway antithrombotic therapy. The similar result in ischemic outcomes is inconsequential, since the trial was not powered to detect such a difference. Any change in clinical practice would require a highly significant difference in a trial adequately powered for ischemic endpoints. Considering that a dual antithrombotic approach would be more costly than DAPT and would require twice-a-day dosing, compared with once-a-day dosing with DAPT, the value of undertaking such a trial is questionable.

C.V. News from ACC 2017

Rivaroxaban vs. Aspirin for Recurrent VTE: Nearly 3400 adults with venous thromboembolism who’d completed 6–12 months of anticoagulation were randomized to daily rivaroxaban (20 or 10 mg) or aspirin (100 mg). At 1 year, rates of symptomatic recurrent VTE were significantly lower with rivaroxaban (1.5% and 1.2%) than with aspirin (4.4%), with no differences in major bleeding across the groups.

Uninterrupted Dabigatran vs. Warfarin for Ablation in Afib: Some 635 patients undergoing atrial fibrillation ablation were randomized to uninterrupted dabigatran or uninterrupted warfarin. The primary endpoint — major bleeding around the time of the procedure and up to 8 weeks afterward — occurred significantly less often with dabigatran than with warfarin (1.6% vs. 6.9% of patients). Thromboembolic events did not differ between the groups.

TAVR vs. Surgery in Severe Aortic Stenosis and Intermediate Surgery Risk: In an 87-site randomized trial, transcatheter aortic-valve replacement (TAVR) with a self-expanding prosthesis was compared with surgery in patients who had severe aortic stenosis and intermediate surgical risk. The primary endpoint, death or disabling stroke at 2 years, occurred in 12.6% of the TAVR group and 14.0% of the surgery group, a nonsignificant difference.

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