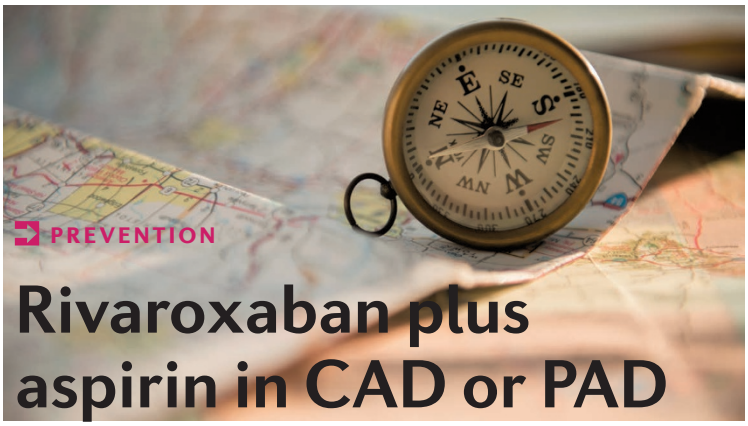
Nature Reviews Cardiology | Published online 30 Nov 2017; doi:10.1038/nrcardio.2017.192



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Rivaroxaban plus aspirin in CAD or PAD

The COMPASS trial was designed to investigate rivaroxaban (a direct factor Xa inhibitor anticoagulant) in addition to, or instead of, aspirin for secondary prevention in patients with atherosclerotic disease. The main results of the trial were presented at the ESC Congress in August 2017. At the AHA Scientific Sessions in November 2017, the COMPASS investigators presented separate analyses in patients with coronary artery disease (CAD) or peripheral artery disease (PAD), and the findings were published in *The Lancet*.

Overall, 24,824 patients with CAD and 7,470 patients with PAD were enrolled in the COMPASS trial. After a 30-day run-in period, all patients were randomly assigned to receive rivaroxaban (2.5 mg twice daily) plus aspirin (100 mg once daily), rivaroxaban only (5 mg twice daily), or aspirin only (100 mg once daily). The trial was halted after the first interim analysis because of clear evidence of efficacy of the combination treatment.

In patients with stable CAD, the combination of rivaroxaban plus aspirin reduced the rate of the primary outcome (myocardial infarction, stroke, or cardiovascular death) more than aspirin alone (HR 0.74, 95% CI 0.65–0.86, $P < 0.0001$), and also reduced mortality (HR 0.77, 95% CI 0.65–0.90, $P = 0.0012$). However, combined treatment resulted in a higher risk of major bleeding than use of aspirin alone (HR 1.66, 95% CI 1.37–2.03, $P < 0.0001$), mainly in the gastrointestinal tract. Rivaroxaban alone did not significantly improve the primary outcome versus aspirin alone, but increased the risk of major bleeding.

Similarly, in patients with PAD, the combination of rivaroxaban plus aspirin compared with aspirin only reduced the occurrence of the primary outcome (HR 0.72, 95% CI 0.57–0.90, $P = 0.0047$), and also major adverse limb events including major amputation (HR 0.54, 95% CI 0.35–0.82, $P = 0.0037$). Again, this benefit was at the expense of an increased risk of major bleeding (HR 1.61, 95% CI 1.12–2.31, $P = 0.0089$), mainly gastrointestinal. Rivaroxaban only compared with aspirin only did not reduce the primary outcome, but did reduce major adverse limb events, also with an increase in major bleeding events.

"A new era of antithrombotic therapy is emerging for patients with PAD," comments Jeffrey S. Berger in an editorial accompanying the trial publication. "Platelet inhibition with or without low-dose anticoagulation will be decided by the ability to balance ischaemic and bleeding risks when selecting the type, dose, and intensity of antithrombotic therapies for individual patients with PAD." In another editorial, E. Magnus Ohman considers which patients will benefit most from combined treatment. "Patients with stable polyvascular disease (CAD with PAD or cerebrovascular disease) have high event rates ... A potential 25% relative reduction in cardiovascular events in these high-risk patients ... would be a great advance in the field of secondary prevention."

Gregory B. Lim

ORIGINAL ARTICLES Connolly, S. J. *et al.* Rivaroxaban with or without aspirin in patients with stable coronary artery disease: an international, randomised, double-blind, placebo-controlled trial. *Lancet* http://dx.doi.org/10.1016/S0140-6736(17)32458-3 (2017) | Anand, S. S. *et al.* Rivaroxaban with or without aspirin in patients with stable peripheral or carotid artery disease: an international, randomised, double-blind, placebo-controlled trial. *Lancet* http://dx.doi.org/10.1016/S0140-6736(17)32409-1 (2017)
FURTHER READING Capodanno, D. *et al.* Antithrombotic therapy for secondary prevention of atherothrombotic events in cerebrovascular disease. *Nat. Rev. Cardiol.* **13**, 609–622 (2016)