**Evolving Landscape of Antithrombotic Therapy for Atherosclerosis**

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Aspirin remains the foundation of antiplatelet therapy. Trials soon to report will clarify its role in primary prevention. The role of aspirin in secondary prevention seems quite secure, though recent data have raised concerns about whether the enteric coating might impede its absorption and antiplatelet effects. Clopidogrel, now generic, remains in common use worldwide for high risk secondary prevention, as monotherapy in patients with myocardial infarction, ischemic stroke, or symptomatic peripheral artery disease. It also remains an important part of dual antiplatelet therapy after stenting in stable coronary artery disease. In acute coronary syndromes, dual antiplatelet therapy seems particularly important for at least a year of therapy, regardless of whether patients are treated with stents or medical therapy; ticagrelor is being used instead of clopidogrel in patients at low bleeding risk. The combination of aspirin with low dose rivaroxaban may soon provide an additional option for stable coronary or peripheral artery disease.

**SETTING A NEW DIRECTION IN CAD AND PAD - THE COMPASS TRIAL**

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The COMPASS trial was based upon the subgroups from CHARISMA where more potent antithrombotic therapy seemed beneficial. A broad range of patients with stable coronary artery disease or stable peripheral artery disease (or both) were enrolled. The control arm used aspirin monotherapy. One experimental arm used rivaroxaban 5 mg twice daily. The other experimental arm used aspirin plus rivaroxaban 2.5 mg twice daily. The combination therapy arm emerged as the winner, with a significant reduction in cardiovascular death, myocardial infarction, or stroke versus aspirin alone. Additionally, in the patients with peripheral artery disease, there was a significant reduction in major adverse limb events and also in major amputations. There was a significant increase in major bleeding, but no significant excess in fatal or intracranial bleeding. Thus, there was a very favorable net clinical benefit for the combination therapy. A subsequent analysis using data from the international REACH registry found that a large percentage of the REACH patients would have been eligible for COMPASS, making the results quite generalizable.