Circulation

The COMPASS Trial: Net Clinical Benefit of Low-Dose Rivaroxaban plus Aspirin as Compared With Aspirin in Patients with Chronic Vascular Disease

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Abstract

Background:

Rivaroxaban 2.5 mg twice daily plus acetylsalicylic acid (aspirin; ASA) 100 mg reduced the risk of cardiovascular events as compared with ASA monotherapy in the COMPASS trial (Cardiovascular Outcomes for People Using Anticoagulation Strategies) but increased the risk of major bleedings. Analysis of net clinical benefit (NCB) is of key clinical relevance and represents an integrated measure of overall patient outcome.

Methods:

The current prespecified analysis was performed to assess the NCB of adding rivaroxaban 2.5 mg twice daily to ASA monotherapy in patients with chronic vascular disease in the COMPASS study cohort (intention-to-treat study population), with a specific focus on high-risk subgroups. The predefined NCB outcome was the composite of cardiovascular death, stroke, myocardial infarction, fatal bleeding, or symptomatic bleeding into a critical organ.

Results:

A lower number of NCB adverse outcomes was observed with rivaroxaban 2.5 mg twice daily plus ASA versus ASA alone (hazard ratio, 0.80 [95% CI, 0.70-0.91], P=0.0005), which became increasingly favorable with longer treatment duration. The main drivers of NCB outcomes were "efficacy" events, in particular stroke (0.5%/y versus 0.8%/y; hazard ratio, 0.58 [95% CI, 0.44-0.76], P<0.0001) and cardiovascular death (0.9%/y versus 1.2%/y; hazard ratio, 0.78 [95% CI, 0.64-0.96], P=0.02), whereas the bleeding components of the NCB, in particular fatal bleeding (0.09%/y versus 0.06%/y; hazard ratio, 1.49 [95% CI 0.67-3.33], P=0.32), only represented a minority of NCB events. In selected high-risk subgroups, including patients with polyvascular disease (≥2 vascular beds affected with atherosclerosis), impaired renal function, heart failure, and/or diabetes mellitus, a larger absolute risk reduction for experiencing a NCB event was observed.

Conclusions:

Compared with ASA monotherapy, the combination of rivaroxaban 2.5 mg twice daily plus ASA resulted in fewer NCB events primarily by preventing adverse efficacy events, particularly stroke and cardiovascular mortality, whereas severe bleedings were less frequent and with less clinical impact. The NCB was particularly favorable in

high-risk subgroups and those with multiple risk characteristics. Registration: URL: https://www.clinicaltrials.gov; Unique identifier: NCT01776424.

Keywords:

Anticoagulation; chronic coronary syndrome; net clinical benefit; rivaroxaban.

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