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ACUTE CORONARY SYNDROMES

APPRAISE-2 RESULTS PUBLISHED

The APPRAISE-2 investigators have published their findings in the *New England Journal of Medicine* 8 months after the phase III trial was terminated prematurely because of unacceptable bleeding rates in the apixaban group. The addition of 5 mg apixaban twice daily to standard antiplatelet therapy in high-risk patients with a recent acute coronary syndrome (within 7 days of trial enrollment) did not result in a significant reduction in recurrent ischemic events.

The international, double-blind, placebo-controlled, randomized clinical trial was halted after 7,315 patients had enrolled and started treatment (3,673 with the oral factor Xa inhibitor apixaban and 3,642 with placebo). The median follow-up duration was 240 and 242 days, and the median exposure to study drug was 175 and 185 days, for patients who received apixaban and those who received placebo, respectively.

No differences between the treatment groups were found for the primary efficacy outcome (a composite of cardiovascular death, myocardial infarction, or ischemic stroke) or for any of the secondary efficacy outcomes. The findings were consistent across all patient subgroups.

At some point between their first dose and 2 days after their last dose of study drug, TIMI major bleeding (the primary safety outcome) occurred in 1.3% of patients who had received at least one dose of apixaban, compared with 0.5% of patients in the placebo group (HR 2.59; 95% CI 1.50–4.46; $P=0.001$). Patients receiving apixaban also experienced more fatal bleeding, intracranial bleeding, ISTH major or clinically relevant nonmajor bleeding, GUSTO severe or moderate bleeding, total bleeding, and transfusions than patients receiving placebo.

Apixaban was not associated with increases in rates of other adverse events assessed, which included events related to hepatoxicity, and gastrointestinal, renal, and respiratory disorders.

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Original article Alexander, J. H. *et al.* Apixaban with antiplatelet therapy after acute coronary syndrome. *N. Engl. J. Med.* doi:10.1056/NEJM0a1105819