

Is Vorapaxar a safe and effective antiplatelet agent for patients with prior Ischaemic Stroke receiving standard antiplatelet therapy?

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Why is the study important?

Atherothrombotic ischaemic strokes account for a large number of strokes and are an important target for secondary prevention. Protease-activated receptor-1 is the main receptor for thrombin on human platelets. Vorapaxar is a potent antagonist of protease-activated receptor-1 that inhibits thrombin-mediated platelet activation.

Who were the participants?

Vorapaxar was evaluated among 26,449 patients with prior atherothrombosis who enrolled in the Thrombin Receptor Antagonist in Secondary Prevention of Atherothrombotic Ischaemic Events-Thrombolysis in Myocardial Infarction (TRA 2[degrees] P-TIMI 50) trial. In the overall cohort Vorapaxar reduced the risk of cardiovascular (CV) death, MI, or stroke by 13%. Specifically this paper looked at the efficacy and safety of Vorapaxar added to standard therapy, for stroke secondary prevention in the 4883 patients with a prior ischaemic stroke.

What were the findings?

For patients who qualified with an ischaemic stroke, the 3-year incidence of CV death, MI, or stroke was 13.0% in the

Vorapaxar group compared with 11.7% in the placebo group; (hazard ratio (HR) 1.03 (95% confidence interval [CI], 0.85-1.25; P=0.75). Recurrent stroke alone was not reduced with Vorapaxar (10.1% vs 7.5%; HR, 1.13; 95% CI, 0.90-1.40; P=0.30). Moderate or severe bleeding was higher in patients treated with Vorapaxar compared with placebo (4.2% vs 2.4%; HR, 1.93; 95% CI, 1.33-2.79).

What were the conclusions?

In this randomized, placebo-controlled, multinational trial, among patients with prior ischaemic stroke, the addition of the Vorapaxar to standard therapy did not reduce the rate of major cerebrovascular events but increased the risk of major bleeding, including intracerebral haemorrhage without a reduction in either the primary efficacy end point or ischaemic stroke alone.

How can this study affect our clinical practice?

The evidence for various combination therapies is slowly increasing for stroke especially referring to antiplatelet therapy. In this sub analysis for a new antiplatelet agent, this combination therapy did not prove to be useful, on the contrary, it produced more harm.

Recommended Reading

1. Efficacy and Safety of Vorapaxar in Patients With Prior Ischemic Stroke. Morrow DA, Alberts M J, Mohr J P, Ameriso S F, Bonaca M P, Goto S, Hankey G J, Murphy S A, Scirica B M, Braunwald E. Stroke 2013; 44: 691-8.

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