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ANTIPLATELET THERAPY

VORAPAXAR IN DIABETES AND MI

Vorapaxar added to standard therapy significantly reduces the risk of major vascular events in patients with diabetes mellitus and previous myocardial infarction (MI), according to an analysis of data from the TRA 2°P-TIMI 50 trial. Vorapaxar is an antagonist of the protease-activated receptor 1 and potently inhibits thrombin-induced activation of platelets via a pathway that is separate from that targeted by aspirin and $P2Y_{12}$-receptor inhibitors. Patients with diabetes are at increased risk of atherothrombotic events, and have increased morbidity and mortality after these events occur. The TRA 2°P-TIMI 50 study was a multinational, double-blind, randomized, placebo-controlled trial of vorapaxar for the secondary prevention of atherothrombosis.

In a prespecified subanalysis, 16,896 patients with a history of MI (but with no history of stroke or transient ischaemic attack, which are contraindications for vorapaxar) were identified. Of these patients, 21% had diabetes. In patients randomly assigned to placebo, diabetes was associated with an increased risk of the primary end point of cardiovascular death, MI, or stroke at 3 years. In patients with diabetes, vorapaxar reduced this end point by 27% compared with control (11.4% vs 14.3%; HR 0.73, 95% CI 0.60–0.89, $P=0.002$). The calculated number needed to treat to prevent one major cardiovascular event over 3 years was 29 among patients with diabetes and 74 among those without diabetes.

Treatment with vorapaxar in patients with diabetes was associated with an increase in moderate or severe bleeding (HR 1.60, 95% CI 1.07–2.40, $P=0.02$), and a similar increase in bleeding was observed with vorapaxar in patients without diabetes. Nevertheless, vorapaxar was of net clinical benefit in patients with diabetes when a combined outcome of cardiovascular death, MI, stroke, recurrent ischaemia leading to revascularization, and moderate or severe bleeding was considered (HR 0.79, 95% CI 0.67–0.93, $P=0.005$). The investigators conclude that "when weighing the risk of bleeding with the antithrombotic benefits of vorapaxar, patients with diabetes appear to be particularly appropriate candidates for consideration of treatment".

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Original article Cavender, M. A. *et al.* Vorapaxar in patients with diabetes and prior MI: findings from the TRA 2°P-TIMI 50 trial. *Circulation* doi:10.1161/CIRCULATIONAHA.114.013774