

## DYSLIPIDAEMIA

## Niacin–laropiprant fails to reduce the risk of vascular events

High-dose niacin has been previously shown to reduce levels of LDL-cholesterol and increase HDL-cholesterol levels, and thereby maintain a low ratio of total to HDL-cholesterol, which is associated with reduced cardiovascular risk. Despite current guidelines promoting niacin therapy for lowering cardiovascular events, the drug's clinical efficacy and safety were uncertain. Investigators in

the HPS2-THRIVE trial have, therefore, conducted the largest study to date evaluating the efficacy of niacin therapy in reducing vascular events.

Over 25,000 participants with vascular disease were assigned to receive either 2 g of extended-release niacin plus 40 mg laropiprant, or a placebo daily. Laropiprant reduces skin flushing, a common adverse effect of niacin therapy, and was administered to improve adherence.

Discontinuation of treatment was significantly greater in the niacin–laropiprant group than in the placebo group (25.4% vs 16.6%;  $P < 0.001$ ). Niacin–laropiprant did not reduce the incidence of major vascular events compared with placebo (13.2% vs 13.7%; rate ratio 0.96, 95% CI 0.90–1.03,  $P = 0.29$ ). However, the rate of serious adverse events was significantly increased in the niacin–laropiprant group compared with placebo (55.6% vs 52.7%;  $P < 0.001$ ). Notably, patients with diabetes mellitus in the niacin–laropiprant arm had a 55% proportional increase in disturbances

in diabetes control compared with patients receiving placebo. In patients receiving niacin–laropiprant who did not have diabetes at randomization, a 32% proportional increase in the diagnosis of diabetes was reported. Other adverse events associated with niacin involved the skin, gastrointestinal system, musculoskeletal system, infection, and bleeding. The investigators conclude that “although niacin might still be relevant for particular patient groups, any potential benefit should be considered in the context of the observed hazards”.

In an accompanying editorial, Donald M. Lloyd-Jones reiterates that “although higher HDL cholesterol levels are associated with better outcomes, it is time to face the fact that increasing the HDL cholesterol level in isolation seems unlikely to offer the same benefit”.

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**Original article** The HPS2-THRIVE Collaborative Group. Effects of extended-release niacin with laropiprant in high-risk patients. *N. Engl. J. Med.* 371, 203–212 (2014)



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