

HPS2-THRIVE: Questions & Answers

What do the results from the HPS2-THRIVE study show?

The main findings were:

- Taking ER niacin/laropiprant on top of statin-based treatment did not reduce the risk of heart attacks, strokes and operations to open blocked arteries
- This result appeared to be similar in all the different types of people taking part in the study
- ER niacin/laropiprant did cause side-effects. Many of these were known before the study (for example, skin irritation and gastrointestinal disturbance). Some were discovered during the study (for example, an increased risk of a rare side-effect of statins called “myopathy” among patients in China). A small increase in risk of other unexpected side-effects was found during analysis of the final results. These included bleeding (into the stomach and also causing strokes) and infections
- There was no effect (either good or bad) on cancer risk nor risk of death

Why are the results from HPS2-THRIVE important?

Niacin treatment has been used for many years to reduce the risk of circulatory disease (i.e. heart attacks, strokes and procedures to open blocked arteries). HPS2-THRIVE shows that ER niacin/laropiprant in fact does not add any benefit on top of current standard treatment and in fact causes more side-effects. This confirms the results of previous smaller studies of niacin which also did not show any benefit, so many thousands of patients who currently take such treatment probably no longer need to do so. However, before anyone stops niacin it is important that they discuss it with their doctor first.

Are the results from HPS2-THRIVE consistent with previous studies?

Yes. A smaller study of 3414 volunteers in America was published in 2011 also showed that niacin (without laropiprant) did not produce any benefit. However, that study was relatively small meaning that a moderate (but important) benefit could not be reliably excluded. However, HPS2-THRIVE was a large study involving over 25,000 people. This means we can be much more confident about its conclusions. There was a study published in the 1970s which showed that niacin did reduce the risk of heart attacks and strokes, but the relevance of this is unclear because this trial was done before many current standard treatments (like statins, aspirin and blood pressure medications) were available or widely used.

Are there any patients who should take ER niacin/laropiprant?

No. The size of HPS2-THRIVE allowed the investigators to explore whether the treatment worked differently in different types of patient (for example, those with or without diabetes). No type of patient was identified that clearly benefited from ER niacin/laropiprant.

Were there any adverse effects of treatment?

Yes. It has long been known that niacin has side effects including skin irritation, gastrointestinal disturbance and elevated blood sugar levels but it was hoped that the benefits in terms of preventing heart disease might outweigh these problems. The laropiprant component of the HPS2-THRIVE treatment was used to reduce the commonest of these side effects, flushing (an unpleasant feeling of warmth in the skin which occurs shortly after taking niacin).

During HPS2-THRIVE it became apparent that ER niacin/laropiprant also increased the risk of the rare side effect of statins called “myopathy” particularly among patients in China. Myopathy is caused by muscle breakdown and causes weak or painful muscles and rarely is severe enough to damage the kidneys (a condition called rhabdomyolysis). Myopathy rapidly gets better when the statin is stopped and no-one in HPS2-THRIVE came to any long-term harm from myopathy. This result was identified during the study and doctors around the world were alerted to it.

During the final analyses it became apparent that ER niacin/laropiprant also increased the risk of some previously unexpected side effects, in particular bleeding and infection. It is not clear at the moment why this happens. More research will be needed to investigate this.

Should people take ER niacin/laropiprant now the study is over?

No. HPS2-THRIVE showed that ER niacin/laropiprant does not reduce the risk of heart attacks and strokes and furthermore it does increase the risk of side effects. Because of the HPS2-THRIVE results, the manufacturer of ER niacin/laropiprant (Merck Sharp & Dohme) have decided to cease making the drug and have suspended it from the market.

Should people take niacin alone in the light of the HPS2-THRIVE results?

Probably not. The similarity between the results of HPS2-THRIVE and previous smaller studies which tested niacin (without laropiprant) means that it is very unlikely that niacin is beneficial. Whether niacin alone causes the same side effects as ER niacin/laropiprant (in particular, the unexpected side effects of bleeding and infection) is less clear and the results of previous studies are being explored to investigate this. People currently taking other ER niacin preparations should discuss these findings with their own doctor.

Can people who took part in HPS2-THRIVE find out whether they received active ER niacin/laropiprant or dummy “placebo” treatment?

We do not plan to routinely tell participants what they received but participants can find out if they wish to. The main reason for not telling people is that it minimises the risk of bias in the assessment of any long-term follow-up of their health. (Someone's knowledge of which treatment they had may affect what they later report.) All participants stopped their study treatment in 2012 and it is very unlikely that knowing what they were taking during the study will have any effect on the care they receive from now on. However, if someone (or their doctor) definitely wants to find out what treatment their patient received, they will be able to do so by contacting the HPS2-THRIVE investigator at their study site or in the UK by calling Freefone 0800585323.

Niacin is washed out of the body very quickly and so there is no reason to suppose that any adverse effects would continue after the tablets were stopped. It is not possible to know whether individuals who experienced side effects did so because of the treatment or because of their heightened risk to heart-related disorders. Anyone with any concerns should discuss them with their GP or with one of the study members of staff.

What happens next?

The main study findings are to be published in a leading medical journal so that the medical community can examine the details of this important study.