New cholesterol-lowering drug could help patients unable to take statins
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A new class of oral cholesterol-lowering drug could help patients unable to take statins due to side effects.

The findings come from the largest study to date to test the effectiveness and safety of bempedoic acid, an oral medication—yet to be approved in Europe—which inhibits the body’s ability to create the building blocks of cholesterol.

The research, published today in the New England Journal of Medicine, reports on findings from more than 2,200 patients and is the first to measure the safety and effectiveness of the new treatment against placebo in patients with increased risk of heart attack and stroke.

According to the group behind the study, the cholesterol-lowering treatment could be added to patients’ existing drug regimens as well as providing an option for people who are unable to tolerate statins due to side effects such as muscle pain or bad interactions with other medications.

Professor Kausik Ray, from Imperial College London’s School of Public Health, who led the study, said: "We know that reducing your cholesterol levels is key to cutting the risk of heart attack and stroke, particularly if you already have established heart disease.

"Our latest study shows that bempedoic acid could be another addition to the arsenal of cholesterol-lowering treatments available to patients. What we have is a new class of drug that could be given to patients who are already taking statins and could help them to further reduce their cholesterol levels and thus potentially cut their risk of heart attacks and strokes."

Too much LDL cholesterol (commonly called "bad cholesterol") in the blood can lead to plaques which clog blood vessels and increase the chance of heart attack and stroke. Many patients at higher risk, such as those with diabetes, inherited conditions or who have previously had heart attack or stroke, are prescribed cholesterol-lowering drugs, like statins, to reduce their risk.

Like statins, bempedoic acid works by blocking a key enzyme used by the body to make cholesterol, in this case an enzyme called ATP-citrate lyase.

In the latest study, a total of 2,230 patients with high cholesterol levels (at least 1.8 mmol/L or 70 mg/dl) and taking cholesterol-lowering drugs (high or moderate intensity dose statins and/or ezetimibe) were randomly chosen to receive either the new treatment or placebo for one year.

Patients were drawn from the UK, Germany, Poland, Canada and the US, and were on varying intensities of cholesterol-lowering treatment.
regimens. The trial also included a small proportion of patients with familial hypercholesterolemia (FH), an inherited condition which causes increased cholesterol levels and raises the risk of cardiovascular disease and strokes.

After three months of treatment researchers found that bempedoic acid reduced patients’ LDL cholesterol levels from baseline by an average of 18.1% compared to the placebo group. In addition, they found that the treatment was effective irrespective of the intensity of the patient's existing cholesterol-lowering treatment.

The treatment was also shown to be well-tolerated by patients, with some increased incidence of gout—due to slight increases in levels of uric acid in the blood—but no increased incidence of serious health conditions between the two groups.

In a second study, also published in the NEJM, the team looked at data from more than half a million people and used genetic markers to model the likely effects of the treatment (blocking the action of the key enzyme ATP citrate) over a longer period and comparing the likely effects to the key enzyme blocked by statins. They found that the effects of inhibiting the enzyme over longer time scale reduced the risk of cardiovascular disease with no obvious adverse effects of blocking this pathway. The benefit was identical to that expected though blocking the enzyme targeted by statins when individuals were matched for change in cholesterol.

Professor Ray added: “One of the key advantages of bempedoic acid is supposed to be that it shouldn’t cause the muscle side effects reported by some statins users, as it taken up by the liver and needs to be converted into its active form via an enzyme only found in the liver. Once converted to the active form the drug cannot leave the liver, so it can't enter muscles and hence could be of considerable advantage for some. It could be an option for patients who are unable to tolerate statins at higher doses, or at all. Our genetic studies suggest that the benefit on prevention of heart disease and strokes in ongoing trials should be identical to that achieved through statins.

"Overall, these latest studies show that not only is the treatment generally well-tolerated being comparable with placebo, and potentially safe over longer periods, but that when added to high intensity statin treatment it can help to further reduce LDL cholesterol levels. The ongoing trial, called ‘CLEAR OUTCOMES’, is specially testing even longer-term safety and whether this approach reduces cardiovascular disease in addition to lowering cholesterol."

The US pharmaceutical company behind the drug, Esperion, is seeking a licence to market the drug this year in Europe and the US.


Provided by Imperial College London

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