Major international study to test new heart disease drug

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CTSU is to lead a major study involving 30,000 people to test a new type of cholesterol treatment.

(PhysOrg.com) -- A major international study to test whether a new type of cholesterol treatment can prevent coronary deaths and heart attacks will start in early 2011. The study will be coordinated by the Clinical Trial Service Unit at Oxford University.

The REVEAL trial will investigate whether a drug called anacetrapib can drive down the risks of coronary deaths, heart attacks and other vascular complications. The study will involve 30,000 people who have some form of heart or other vascular disease from the UK, North America, China, Germany, Italy, Scandinavia and elsewhere.

REVEAL is being funded by Merck Sharp & Dohme, which developed

anacetrapib. A grant of £96 million towards the cost of this multi-million dollar study has been provided to the University of Oxford. This is the largest single research contract ever entered into by the University.

Professor Andrew Hamilton, Vice Chancellor of Oxford University, said: 'I am delighted that Oxford's Clinical Trial Service Unit will run this major international trial. The new project on such a large scale reinforces Oxford medicine's position at the forefront of international research. The University has built up the skills and expertise over many years to independently undertake these complex – and very important – clinical trials, the results of which can potentially save millions of lives around the world.'

CTSU is well known for running huge international studies, including the ground-breaking Heart Protection Study which showed that a third of all heart attacks and strokes can be safely avoided in people at risk of vascular disease by using statins to lower 'bad' LDL cholesterol. The unit also showed that more intensive lowering of LDL cholesterol with statins safely produces extra benefits.

A new type of cholesterol drug

Anacetrapib is a new type of cholesterol treatment, belonging to a drug class known as CETP (cholesteryl ester transfer protein) inhibitors, which is being developed by Merck Sharp & Dohme. It has been found to produce substantial reductions in blood levels of 'bad' LDL cholesterol (equivalent to, and additional to, those achieved with statin drugs), and it more than doubles 'good' HDL cholesterol levels.

Anacetrapib has been studied in about 2,000 people, of whom about 500 have taken it for 18 months. In that research, led by a team from Brigham and Women's Hospital in Boston, anacetrapib was not associated with adverse effects on any of the key safety endpoints,

including blood pressure or other vascular risk factors. The results were reported yesterday in the New England Journal of Medicine and at the American Heart Association conference in Chicago.

Large randomized studies have shown that lowering LDL cholesterol by 1 mmol/L for 4–5 years with statin therapy cuts the risks of heart attacks and strokes by about a quarter, and recent studies suggest that more intensive LDL-lowering can produce extra benefits. But, despite the use of statins, the risk of heart attacks, strokes and other vascular complications among people who have vascular disease remains high.

Previous studies have also shown that people with high blood levels of HDL cholesterol tend to have fewer heart attacks or coronary deaths. However, there is limited evidence of any benefits with the drugs that are currently available to raise HDL cholesterol, and widespread use of the most effective of these HDL-raising drugs – which is called niacin – is limited by side-effects and poor tolerability.

The new trial

Dr Martin Landray of Oxford University, one of the co-principal investigators of REVEAL, said: ‘This study could mark the start of a new era of cholesterol treatment. Anacetrapib has really dramatic effects on blood levels of cholesterol, even in those already on a statin, and it appears to be well tolerated.

‘The key question now is whether these cholesterol changes prevent coronary deaths and heart attacks. It is also critical to determine whether there are any unexpected side-effects over the longer term. The potential is massive, but we need a really large trial to provide a definitive answer – REVEAL is that trial.’

Dr Louise Bowman of Oxford University, the other co-principal

investigator, said: ‘This is a very exciting opportunity to try and improve life for the millions of people who have, or will develop, heart disease in the years to come.

‘Large studies like REVEAL are vital if we are to discover new, safe and effective ways to reduce further the suffering caused by heart attacks, strokes and risky heart artery by-pass procedures.

‘If the impressive effects of anacetrapib on cholesterol levels are translated into fewer deaths and heart attacks, then this treatment has the potential to produce substantial benefit for patients.’

REVEAL is a huge research undertaking and will take more than 6 years to complete, involving doctors and nurses in about 400 hospitals around the world. It will recruit 30,000 men and women aged at least 50 with a history of heart attack, stroke or peripheral arterial disease.

Oxford’s CTSU has designed the study and will be responsible for coordinating it and analysing its results, independently of the funders. A steering committee of international academic experts, chaired by Professor Rory Collins from Oxford University, will be responsible for the overall running of the study.

CTSU will be the central coordinating centre, with 6 regional coordinating centres initially in the UK, North America, China, Germany, Italy and Scandinavia. The TIMI research group in Boston, led by Professor Eugene Braunwald will coordinate the North American part of the study.

Professor Jeremy Pearson, Associate Medical Director at the British Heart Foundation, said: ‘This is an important trial, led by BHF-funded researchers. Few drugs raise “good” cholesterol as well as lowering “bad”, but CETP inhibitors do both. This research will show whether this

drug can improve chances of survival, potentially giving new hope for millions of people whose cholesterol levels put them at serious risk of heart disease.'

Provided by Oxford University