

**EMBARGO: 08:30 Central European Summer Time Tuesday 29th August 2017**

## **ANACETRAPIB REDUCES THE RISK OF SERIOUS CARDIOVASCULAR EVENTS AMONG HIGH-RISK PATIENTS ON INTENSIVE STATIN TREATMENT**

**Barcelona, Tuesday 29 August 2017:** Anacetrapib, an inhibitor of Cholesteryl Ester Transfer Protein (CETP) activity, lowers the risk of heart attack and related cardiovascular complications among patients who are receiving intensive statin treatment. These are the conclusions from a major randomized controlled trial of 30,000 participants led by researchers in the Clinical Trial Service Unit at the University of Oxford.

Unveiling the key findings at the European Society of Cardiology Congress today, the trial's co-principal investigator Professor Martin Landray said:

“The REVEAL trial has shown for the first time that adding anacetrapib to intensive statin therapy reduces the incidence of cardiovascular events for high risk patients. The treatment was very well tolerated and there were no major safety concerns.

“These findings are in marked contrast to the disappointing results of previous trials of other CETP inhibitors. The reduction in the risk of cardiovascular events is in line with the effects of other drugs that lower LDL cholesterol levels, such as statins. The large increase in HDL cholesterol levels produced by anacetrapib did not appear to have much impact on risk.”

The Randomized Evaluation of the Effects of Anacetrapib through Lipid Modification (REVEAL) trial involved over 30,000 men and women who had some form of vascular disease, such as heart attack or stroke. They were recruited from more than 400 hospitals in the UK, USA, Canada, China, Germany, Italy, and Scandinavia. All participants were given intensive treatment with atorvastatin (a commonly prescribed statin drug) to ensure good control of LDL (“bad”) cholesterol. Participants also received anacetrapib, an investigational CETP inhibitor, or a matching placebo for an average of 4 years. Information was recorded on cardiovascular events, death, cancer, reasons for hospital admission, and a wide range of other health-related outcomes relevant to understanding the safety and efficacy of anacetrapib.



The REVEAL study results are summarized below:

- Adding anacetrapib to statin therapy reduced the blood level of LDL cholesterol by around 20% and doubled the level of HDL cholesterol.
- Adding anacetrapib to intensive statin treatment produced a 9% proportional reduction in the risk of the composite outcome of heart attack, death from heart disease, or coronary revascularization (i.e. coronary artery stenting or bypass surgery).
- In a subsidiary analysis, anacetrapib significantly reduced the composite outcome of coronary death or myocardial infarction. There was no significant effect on ischaemic stroke.
- Anacetrapib was well tolerated and, as has been found previously, the levels of anacetrapib in body fat continued to increase while treatment continued.
- Anacetrapib produced a small reduction in the risk of developing diabetes mellitus.
- There were no major safety signals and no increase in death, cancer or other serious medical events, but there was a small increase in blood pressure and a small reduction in kidney function.

The main results are published in more detail in the [New England Journal of Medicine](#) today.

The positive results of the REVEAL trial of 4 years of anacetrapib treatment contrast with the results of previous trials of other CETP inhibitors, all of which were stopped after about 2 years of follow-up due to either unexpected hazards or apparent lack of efficacy.

Dr Louise Bowman, the other co-principal investigator of REVEAL, explained:

“The REVEAL trial has a number of strengths which allow reliable assessments of both efficacy and safety. It recruited around twice as many participants as any previous trial of a CETP inhibitor; it collected information on double the number of cardiovascular events; and the CETP inhibitor treatment continued for twice as long.

“The full effects of anacetrapib did not appear to emerge until beyond the first year of treatment. A similar pattern has been observed in randomized trials of other LDL-cholesterol lowering treatments, such as statins. Consequently, previous trials of CETP inhibitors that were stopped after only about 2 years may have been too short for any benefits to emerge.”

The REVEAL trial was designed and conducted by independent investigators (supported by the British Heart Foundation and Medical Research Council) in the Clinical Trial Service Unit at the University of Oxford, Oxford, UK, in collaboration with the Thrombolysis in Myocardial Infarction (TIMI) Study Group at Brigham and Women's Hospital and Harvard Medical School in Boston, USA, along with other members of the independent academic Steering Committee and MSD (known as Merck in the USA and Canada). MSD also funded the trial and provided the study drugs.

Professor Landray acknowledged all those who contributed to the success of the study:

“We would particularly like to thank the 30,000 patient volunteers who participated in REVEAL. It would also not have been possible without the efforts of hundreds of clinicians and researchers from around the world. Together they have made it possible to demonstrate that heart disease risks can be reduced further by adding anacetrapib to current therapy.”

#### **Additional Quotes**

Professor Sir Rory Collins of University of Oxford, Chair of the REVEAL Steering Committee:

“The results of the REVEAL study are encouraging. The participants had very low levels of LDL cholesterol to start with. Even so, adding anacetrapib to the intensive statin therapy not only lowered LDL cholesterol levels further, but it also reduced the risks of heart attacks and of other major cardiovascular outcomes without major safety concerns.”

Professor Eugene Braunwald of the TIMI Study Group at Brigham and Women's Hospital and Harvard University in Boston, USA, Deputy Chair of the REVEAL Steering Committee:

“Cardiovascular disease remains a leading cause of death and disability for patients and a major burden for health care systems. REVEAL shows that anacetrapib can further reduce the risks of major cardiovascular outcomes even among people who are already being treated in accordance with current guidelines.”

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Professor Jeroen Bax of Leiden University Medical Center, President of the European Society of Cardiology:

“The results of the REVEAL trial demonstrate the power of clinical, academic and industry collaboration on an international scale and the benefits this can bring to medical science and the safe and effective care of patients with heart disease.”

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**Notes:**

The results of the REVEAL trial have been published in the New England Journal of Medicine today and are freely available at [www.nejm.org](http://www.nejm.org) or via the REVEAL website at [www.revealtrial.org](http://www.revealtrial.org)

[REVEAL](#) involved 30,000 men and women aged at least 50 with a history of heart disease, stroke or peripheral artery disease. About one-third also had a history of diabetes. All study participants received intensive treatment with atorvastatin, (a commonly used ‘statin’ drug) to ensure good control of LDL (“bad”) cholesterol. They were randomly allocated to receive anacetrapib (100 mg daily) or matching placebo (dummy) tablets daily for an average of 4 years. The primary aim of the study was to find out whether the participants allocated to receive anacetrapib would be less likely to suffer a heart attack, have a coronary revascularization procedure (coronary stenting or bypass surgery) or die from heart disease than those allocated to receive placebo control treatment.

REVEAL is conducted by an international collaboration between the [Clinical Trial Service Unit](#) at the University of Oxford; the TIMI Study Group at Brigham & Women’s Hospital and Harvard Medical School in Boston, MA; the University Hospital and University of Würzburg in Würzburg, Germany; the Associazione Nazionale dei Medici Cardiologi Ospedalieri (ANMCO) in Florence, Italy; the China-Oxford Centre for International Health Research of Fuwai Hospital, Chinese Academy of Science National Center for Cardiovascular Disease in Beijing, China; and investigators in Denmark, Finland, Norway and Sweden.

The University of Oxford holds the study database and conducts the statistical analyses for all publications, presentations and regulatory submissions. The independent Steering Committee is responsible for drafting the main reports from the study and for review of any other reports. The study Steering Committee includes representatives from the central and regional coordinating centres, cardiologists, clinical trialists, and statisticians. MSD has non-voting membership on the Steering Committee, and provides trial coordination within Scandinavia through its subsidiaries under the direction of, and monitored by, the University of Oxford.

The [Clinical Trial Service Unit](#) at the University of Oxford receives support from the UK Medical Research Council (which funds the [MRC Population Health Research Unit](#) in a strategic partnership with the University of Oxford) and the British Heart Foundation. Within the UK, the REVEAL trial sites received support from the National Institute for Health Research Clinical Research Network.

The Clinical Trial Service Unit at the University of Oxford has a staff policy of not accepting honoraria or consultancy fees, either to staff or the institution, directly or indirectly from industry (see [https://www.ctsu.ox.ac.uk/files/research/ctsu-independent-research\\_27june14.pdf](https://www.ctsu.ox.ac.uk/files/research/ctsu-independent-research_27june14.pdf)).

#### About the Medical Research Council (MRC)

The Medical Research Council is at the forefront of scientific discovery to improve human health. Founded in 1913 to tackle tuberculosis, the MRC now invests taxpayers' money in some of the best medical research in the world across every area of health. Thirty-one MRC-funded researchers have won Nobel prizes in a wide range of disciplines, and MRC scientists have been behind such diverse discoveries as vitamins, the structure of DNA and the link between smoking and cancer, as well as achievements such as pioneering the use of randomised controlled trials, the invention of MRI scanning, and the development of a group of antibodies used in the making of some of the most successful drugs ever developed. Today, MRC-funded scientists tackle some of the greatest health problems facing humanity in the 21st century, from the rising tide of chronic diseases associated with ageing to the threats posed by rapidly mutating micro-organisms. [www.mrc.ac.uk](http://www.mrc.ac.uk)

#### About the British Heart Foundation (BHF)

For over 50 years we've pioneered research that's transformed the lives of people living with heart and circulatory conditions. Our work has been central to the discoveries of vital treatments that are changing the fight against heart disease. But so many people still need our help. From babies born

**EMBARGO: 08:30 Central European Summer Time Tuesday 29th August 2017**

with life-threatening heart problems to the many Mums, Dads and Grandparents who survive a heart attack and endure the daily battles of heart failure. Every pound raised, minute of your time and donation to our shops will help make a difference to people's lives. For more information, visit [www.bhf.org.uk](http://www.bhf.org.uk).

Anacetrapib is an investigational medicine. It is not licensed or available for clinical use at present.

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