



**PRESS RELEASE**  
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**MONTREAL HEART INSTITUTE RESEARCH  
FEATURES PROMINENTLY AT AMERICAN COLLEGE  
OF CARDIOLOGY 56<sup>TH</sup> ANNUAL SCIENTIFIC SESSION**

**MHI led major late-breaking clinical trials on HDL properties  
and on novel anti-oxidant and anti-inflammatory agent**

**Montreal, April 4, 2007** – The Montreal Heart Institute (MHI), recognized worldwide for its strong commitment to research, seized the opportunity to consolidate its leadership in the field when it unveiled the results of two late-breaking clinical trials at the American College of Cardiology’s (ACC) 56<sup>th</sup> Annual Scientific Session, held in New Orleans March 24-27.

The trials, known by their acronyms ERASE and ARISE, were led by Dr. Jean-Claude Tardif, Director of Research Center at the MHI and Professor of Medicine at the Université de Montréal. Dr. Tardif was also the co-principal investigator in another major study, ILLUSTRATE, whose findings were unveiled at the ACC as well.

“The results of the three studies have generated tremendous interest in the scientific and medical communities and are already leading us to plan the next phases of investigations,” Dr. Tardif said. “The MHI Research Centre is proud to share with the scientific community the latest discoveries in treatment and prevention of cardiovascular diseases.”

**Results from the ERASE study**

***Drug that mimics “good cholesterol” has promising effect on coronary atherosclerosis***

Patients with acute coronary syndromes (ACS), such as heart attack and recent-onset chest pain, remain at considerable risk of experiencing further serious cardiovascular problems despite improvements in care. High-density lipoprotein cholesterol or HDL (so-called “good” cholesterol has properties that may protect these patients from further complications by reducing plaque in their coronary arteries.

The results of the ERASE (Effect of Reconstituted High-Density Lipoprotein on Atherosclerosis – Safety and Efficacy) trial showed that CSL-111, a drug that resembles natural HDL, reduced plaque in coronary arteries versus baseline in patients with a recent episode of ACS, although the difference did not achieve statistical significance versus placebo for this endpoint. Patients taking the drug also showed improvement in two indexes (on ultrasound and angiography) that assess changes in the blood vessels ERASE was coordinated by the MHI, with 17 sites throughout Canada. This randomized, blinded clinical trial included 183 patients who had suffered an ACS event within the previous two

weeks. The study appeared online on March 26 on the *Journal of the American Medical Association (JAMA)* website.

According to Dr. Tardif, elevation of HDL remains a valid target in atherosclerosis and further evaluation of the effects of HDL infusions with CSL-111 on clinical outcomes is warranted.

### **Results from the ARISE study**

#### ***Novel anti-oxidant and anti-inflammatory agent shows effectiveness on key endpoints in cardiovascular outcomes***

Heart attacks are caused by a build-up and instability of plaque in the coronary arteries, which is often a result of chronic inflammation of the blood vessel walls. The ARISE (Effects of the Novel Anti-Oxidant and Anti-Inflammatory Agent Succinobucol on Clinical Events in Patients With a Recent Acute Coronary Syndrome: The Aggressive Reduction of Inflammation Stops Events) study assessed whether adding a novel agent with antioxidant and anti-inflammatory properties to optimal medical therapy would reduce coronary events and death among patients with heart disease.

While the trial results did not demonstrate a difference with the use of succinobucol (AGI-1067) versus placebo on the primary endpoint of a composite of adverse cardiovascular events, the study did achieve a reduction in the composite of “hard” atherosclerotic clinical endpoints, composed of cardiovascular death, myocardial infarction (heart attack) and stroke with a relative risk reduction of 19%; as well as an improvement in several key diabetes parameters, including fewer patients developing diabetes with a relative risk reduction of 64% and better glycemic control in patients randomized to succinobucol.

“We are pleased with the meaningful improvement of patient outcomes observed with succinobucol in the ARISE trial, which should help to address the burden of cardiovascular risk that exists despite our effective contemporary treatments.” said Dr. Tardif. “Although the formal primary composite endpoint in ARISE was not met, we believe that the trial generated strong evidence that use of succinobucol will produce tangible clinical benefits for patients with coronary artery disease.”

The double-blind, placebo-controlled international trial enrolled 6,144 high-risk cardiovascular patients with unstable angina (chest pain) or who had suffered a heart attack. The MHI worked in collaboration with the Brigham and Women’s Hospital for this study.

### **Results from the ILLUSTRATE study**

#### ***Despite significantly raising HDL, torcetrapib failed to slow the progression of coronary plaques***

Investigators reported during the ACC Scientific Session that torcetrapib, a drug that substantially raises HDL, or “good” cholesterol, did not slow the progression of plaque build-up in the coronary arteries as measured using an ultrasound probe (IVUS). All development of this drug was terminated on December 2, 2006 after the safety board

monitoring a separate large clinical outcomes trial reported that torcetrapib increased the risk of death and other adverse cardiovascular outcomes.

The results of the ILLUSTRATE (Investigation of Lipid Level management using coronary UltraSound To assess Reduction of Atherosclerosis by CETP Inhibition and HDL Elevation) study are considered pivotal in determining whether the failure of torcetrapib was the result of specific drug toxicity. The development of drugs to raise HDL has been a research priority because, despite lowering LDL (low-density lipoprotein, or “bad” cholesterol) with statin drugs, many patients continue to experience heart attacks, stroke or sudden cardiac death.

A total of 1,188 coronary artery disease patients were enrolled in this trial in which the MHI acted as one of the lead institutions. The torcetrapib/atorvastatin combination markedly increased good cholesterol levels and lowered bad cholesterol. Yet this drug substantially raised blood pressure, an undesirable effect, and failed to slow the build up of plaque. Whether this failure represents a problem unique to torcetrapib or suggests a lack of efficacy for the entire class of similar drugs remains to be determined. This study was published in the *New England Journal of Medicine* on March 29<sup>th</sup> 2007.

### **About the Montreal Heart Institute**

Founded in 1954, the Montreal Heart Institute constantly aims for the highest standards of excellence in the cardiovascular field through its leadership in prevention, ultra-specialized care, training of professionals, clinical and fundamental research, and assessment of new technologies. It is affiliated with the Université de Montréal and its clinical outcomes are among the best in the world. The MHI Research Centre officially came into existence in 1976 and has made enormous strides since its creation. Today, there are approximately 450 employees, students and researchers at the MHI Research Center. The MHI’s outstanding feature is the balance it achieves between basic research, clinical research and clinical care. Its prime focus areas of research are vascular diseases, myocardial function and electrophysiology. Genetics, genomics (including pharmacogenomics), biomarkers and preventive cardiology are other areas of focus. To learn more about the Institute, please visit our website at [www.icm-mhi.org](http://www.icm-mhi.org).

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