A world first: Discovery of a personalized therapy for cardiovascular disease

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Researchers at the Montreal Heart Institute announced today results showing that patients with cardiovascular disease and the appropriate genetic background benefit greatly from the new medication dalcetrapib, with a reduction of 39% in combined clinical outcomes including heart attacks, strokes, unstable angina, coronary revascularizations and cardiovascular deaths. These patients also benefit from a reduction in the amount of atherosclerosis (thickened walls) in their vessels. The detailed results are published in the prestigious journal *Circulation Cardiovascular Genetics*. This discovery may also pave the way for a new era in cardiovascular medicine, with personalized or precision drugs.

The team led by Drs Jean-Claude Tardif and Marie-Pierre Dubé performed the analysis of 5749 patients who received dalcetrapib or placebo and provided DNA in a clinical study. A strong association was discovered between the effects of dalcetrapib and a specific gene called ADCY9 (adenylate cyclase 9) on chromosome 16, particularly for a specific genetic variant (rs1967309). In patients with the genetic profile AA at rs1967309, there was a 39% reduction in the composite cardiovascular endpoint with dalcetrapib compared to placebo. Supporting evidence was also obtained from a second study, which showed that patients with the favourable genetic profile also benefited from a reduction in the thickness of their carotid artery walls with dalcetrapib.

"These results will lead to a genetics-guided clinical study in patients with the appropriate genetic background to allow review by health

regulatory agencies and to provide personalized therapy with dalcetrapib. It also offers great hope for precision treatments for patients with cardiovascular diseases and for curbing atherosclerosis, the first cause of mortality in the world" said lead investigator Jean-Claude Tardif MD, director of the Research Center at the Montreal Heart Institute and professor of medicine at the University of Montreal.

The investigators tested multiple genetic markers across the entire genome in a procedure called genome-wide association study. "We used state-of-the-art genetic and statistical techniques to demonstrate that the effect of the patient's genetic profile was only observed in those treated with dalcetrapib and not placebo. We want to provide patients with additional personalized cardiovascular therapies in the years to come, for more efficacious and safer medicines", commented Marie-Pierre Dubé PhD, director of the Beaulieu-Saucier Pharmacogenomics Center at the Montreal Heart Institute and professor of medicine at the University of Montreal.

More information: To read the article: circgenetics.ahajournals.org/c … .114.000663.full.pdf

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