

## Genetics Guide Personalised Cardiovascular Therapy



New research from Montreal Heart Institute (MHI) has found that cardiovascular patients with a specific genetic profile benefit greatly from the new medication dalcetrapib. The drug reduced heart attacks, strokes, unstable angina, coronary revascularisations and cardiovascular deaths by as much as 39 percent. The findings could pave the way for a new type of cardiovascular medicine, using personalised drugs to target diseases with greater precision.

The MHI team was led by Dr. Jean-Claude Tardif and Dr. Marie-Pierre Dubé, who analysed more than 5,700 cardiovascular patients who provided DNA samples and received either dalcetrapib or a placebo medicine. The research team tested multiple genetic markers across the entire human genome using a procedure called genome-wide association study. The study showed that cardiovascular disease was reduced in certain patients with a favourable genetic profile when those patients were assigned dalcetrapib instead of placebo.

Specifically, there was a strong association between dalcetrapib's success and the ADCY9 gene on chromosome 16, and in particular for the genetic variant rs1967309. Patients with the profile AA at that variant who were assigned dalcetrapib instead of placebo had a 39 percent reduction in the composite cardiovascular endpoint. Further research found that patients with the same genetic profile also experienced reduced thickness in their carotid arteries with dalcetrapib, indicating the drug's potential benefit for atherosclerosis treatment.

Dr. Tardif, a professor of medicine at the University of Montreal and director of the Research Center at MHI, was pleased with the findings. "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 personalised therapy with dalcetrapib," he said. "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."

Dr. Marie-Pierre Dubé, PhD, who directs the Beaulieu-Saucier Pharmacogenomics Center at MHI and is a professor of medicine at the University of Montreal, noted that the study offers hope for patients around the world. "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," she said. "We want to provide patients with additional personalised cardiovascular therapies in the years to come, for more efficacious and safer medicines."

The detailed results have been published in the journal *Circulation: Cardiovascular Genetics*.

Source: MHI (embed <https://www.icm-mhi.org/en>)

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