

Results of the GIANT trial reported

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According to a new study, genetic profiling of patients undergoing percutaneous coronary intervention (PCI) may help cardiology teams adjust treatment and improve ischemic outcomes for patients that do not properly metabolize thienopyridine blood thinning therapies such as clopidogrel.

Findings from the GIANT trial were presented today at the 25th annual Transcatheter Cardiovascular Therapeutics (TCT) scientific symposium. Sponsored by the Cardiovascular Research Foundation (CRF), TCT is the world's premier educational meeting specializing in interventional cardiovascular medicine.

The effectiveness of [clopidogrel](#) depends on activation to an active metabolite, principally via the CYP2C19 enzymatic pathway. Acute coronary syndrome [patients](#) that carry a CYP2C19 gene variant poorly metabolize the drug. These patients are known as slow responders and exhibit a higher one year risk of major ischemic events following PCI. Genetic tests can help identify a patient's CYP2C19 genotype, but it is unknown if on-line adjustment of thienopyridine [therapy](#) in the genetically slow-responder patient population may counteract this outcome.

The GIANT trial evaluated the clinical impact of CYP2C19 [genetic profiling](#) and compliance to an adjusted thienopyridine treatment. The primary endpoint was a composite of death, myocardial infarction, and stent thrombosis after one year in slow responder patients with appropriate therapy after genotyping, compared to non-slow responders.

The prospective, multicenter, single arm study enrolled 1,499 patients at the time of primary PCI (onset chest pain

Strong recommendations for treatment adjustment were sent to investigators when patients were identified as slow responders.

Dual antiplatelet therapy (DAPT) was prescribed for 12 months after PCI and one year follow up was performed in 96.4 percent of patients (n=1,445) including objective assessment of compliance. A total of 22 percent of patients (n=319) had a profile associated with a CYP2C19 loss of function, known as the slow responder group. The remaining patients constituted the control group.

In the slow responder group, 85 percent received an adjusted thienopyridine regimen after the release of the genetic profile. Within the slow responder group, the patients that did receive adjusted therapy experienced fewer adverse events compared to those that did not have adjusted therapy (3.3 percent vs. 15.6 percent, respectively) after one year. Further, the patients that received adjusted therapy experienced a similar rate of adverse events as the control group (3.3 percent vs. 3.04 percent). Poor compliance to treatment was objectively identified in 4.9 percent of patients at one year, and those patients experienced numerically more ischemic events.

"Results from the GIANT trial suggest that in patients with acute [myocardial infarction](#) treated with primary PCI, identification of a slow response to clopidogrel with subsequent adjustment of treatment leads to similar one year major ischemic event rates to patients with a favorable genetic profile to clopidogrel response," said lead investigator Bernard R. Chevalier, MD from L'Institut CardioVasculaire Paris-Sud in Massy, France.

"These findings may help determine alternative treatment strategies for

patients identified as CYP2C19 poor metabolizers."

Provided by Cardiovascular Research Foundation

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