Antiplatelets: 1 person, 1 dose?

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An international consortium of scientists, including major contributions from the Montreal Heart Institute, demonstrates that the "one-size fits all" strategy of uniformly doubling the dose of an antiplatelet drug, clopidogrel, for patients with high on-treatment platelet reactivity does not reduce the incidence on death, heart attacks and stent thrombosis after percutaneous coronary intervention (PCI). The results of the GRAVITAS trial conducted to determine whether high-dose clopidogrel is superior to standard-dose therapy for the prevention of cardiovascular events after percutaneous coronary intervention in patients with high on-treatment reactivity, have been published recently in the *Journal of the American Medical Association*.

The GRAVITAS (Gauging Responsiveness with A VerifyNow assay - Impact on Thrombosis And Safety) study showed no benefit of double-dose compared with standard-dose clopidogrel and the results refute the strategy of uniformly doubling the dose of clopidogrel over six months for patients with high on-treatment platelet reactivity after PCI with drug-eluting stent. In the multicenter, randomized, double-blind, active-control trial, the use of high-dose compared with standard-dose clopidogrel did not reduce the incidence of adverse cardiac events such as death, nonfatal myocardial infarction or stent thrombosis.

"The results of GRAVITAS are surprising because they do not support a uniform treatment strategy of high-dose clopidogrel in patients with high on-treatment reactivity." said Dr. Jean-François Tanguay, interventional cardiologist at the Montreal Heart Institute, professor of medicine at the Université de Montréal and lead investigator in Canada. "Personalized medicine merits further investigation. We need to assess alternative treatment strategies incorporating platelet function testing as opposed to prescribe a fixed, higher dose."

Between July 2008 and April 2010, 2214 patients from 83 sites in North America had high on-treatment reactivity after being screened with platelet function testing 12 to 24 hours after PCI. They were randomly assigned to either higher (double-dose) or standard-dose clopidogrel for six months after drug-eluting stent implantation. An additional 586 patients without high on-treatment reactivity were selected at random and assigned to treatment with standard-dose clopidogrel. Clopidogrel exposure prior to enrollment was similar across all 3 treatment groups.

At six months, the rate of death from cardiovascular causes, nonfatal myocardial infarction or stent thrombosis was not different with high-dose (25 of 1109 patients) compared with standard-dose (25 of 1105 patients) clopidogrel in patients with high on-treatment reactivity. "These low event rates reflect the excellent results we can obtain with drug-eluting stents" said Dr. Tanguay.

More information: 1: Price MJ, Berger PB, Teirstein PS, Tanguay JF, Angiolillo DJ, Spriggs D, Puri S, Robbins M, Garratt KN, Bertrand OF, Stillablower ME, Aragon JR, Kandzari DE, Stinis CT, Lee MS, Manoukian SV, Cannon CP, Schork NJ, Topol EJ; GRAVITAS Investigators. Standard- vs high-dose clopidogrel based on platelet function testing after percutaneous coronary intervention: the GRAVITAS randomized trial.
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