



## **CLOPIDOGREL IMPROVED CORONARY PERFUSION AND REDUCED MORTALITY IN ACUTE HEART ATTACK**

### **Results from two major clinical trials presented at ACC**

**(PARIS and PRINCETON, NJ, MARCH 9, 2005)** – Results of two major clinical trials showed that the antiplatelet agent clopidogrel, given on top of standard therapy, provided significant benefits to patients with acute ST-segment elevation myocardial infarction (STEMI), a certain kind of heart attack. Results of the COMMIT/CCS-2 (CLOpidogrel and Metoprolol in Myocardial Infarction Trial) and CLARITY – TIMI 28 (CLOpidogrel as Adjunctive Reperfusion Therapy - Thrombolysis In Myocardial Infarction Study 28) trials, which included a total of nearly 50,000 patients, were presented today in Orlando, Florida at the 54th Annual Scientific Session of the American College of Cardiology (ACC).

In the **CLARITY-TIMI 28** trial, clopidogrel added to standard therapy including fibrinolytics and ASA (aspirin) reduced the odds of acute MI patients having another occluded artery, or a second heart attack or death by 36 percent after one week of hospitalization (Event rate: 15.0% in clopidogrel arm vs. 21.7% in placebo;  $P < 0.001$ ). Additionally, at thirty days, clopidogrel reduced the odds of clinical events (cardiovascular death, recurrent myocardial infarction, recurrent ischemia leading to urgent revascularization) in these patients by 20 percent (Event rate: 11.6% vs. 14.1%;  $P = 0.03$ ). The results observed with clopidogrel in this clinical setting were consistent irrespective of patients' gender, the standard therapy they received (type of fibrinolytic or type of heparin) or the location of their MI. The CLARITY-TIMI 28 trial enrolled 3,491 patients at 319 sites in 23 countries in North America, Latin America and Europe. The trial was coordinated by the TIMI (Thrombolysis In Myocardial Infarction) Group, chaired by Eugene Braunwald, MD, Distinguished Hersey Professor of Medicine, Harvard Medical School and of Brigham and Women's Hospital.

“Re-occlusion of coronary arteries in acute MI patients has been shown to occur quite frequently,” said Dr. Braunwald. “The CLARITY-TIMI 28 trial demonstrated treating acute MI patients with clopidogrel, on top of standard therapy including aspirin and fibrinolytics, resulted in a 36 percent reduction in the odds of a blocked artery or death or recurrent myocardial infarction by the time of angiography.”

In the **COMMIT/CCS-2** trial clopidogrel, on top of standard therapy including ASA, reduced mortality in acute MI patients. In the 28 days following randomization, clopidogrel reduced the relative risk of death in these patients by 7 percent (Event rate: 7.5% vs. 8.1%;  $P = 0.03$ ). In the same patient population, clopidogrel reduced the relative risk of the combination of recurrent MI, stroke or death by 9 percent (Event rate: 9.3% vs. 10.1%;  $P = 0.002$ ).

The COMMIT/CCS-2 trial, one of the largest randomized double-blind placebo-controlled clinical trials of drug therapy ever conducted in heart disease, enrolled nearly 46,000 patients at 1,250 sites in China. The trial was co-ordinated by Oxford University, UK and the Fuwai Hospital, the Chinese Academy of Medical Sciences, China, and was co-chaired by Rory Collins MD and LS Liu MD.



“The COMMIT/CCS-2 study findings showed that clopidogrel reduced mortality in an in-hospital setting,” added Zheng Ming Chen, MD, University of Oxford. “The study also showed that there was no significant increase in the risk of fatal or transfused bleeding associated with clopidogrel therapy.”

In both trials, the rates of major bleeding and intracranial hemorrhage were similar in both treatment groups. In the CLARITY – TIMI 28 study, there was no statistically significant difference in the incidence of major bleeding and primary intracranial hemorrhage. The rate of major bleeding in the clopidogrel group was 1.3 percent compared with 1.1 percent in the placebo group (p=0.64), on top of the standard therapy group (including fibrinolytics and ASA). In COMMIT/CCS-2, no significant increase in the risk of fatal or transfused bleed was observed. The rate of major, non-cerebral bleeding was 0.4 percent in the clopidogrel compared with 0.3 percent in the placebo on top of standard therapy group including ASA (p=0.52). Additionally, the rate of intracranial hemorrhage was very low and similar in the clopidogrel and placebo groups.

Of the 10 million estimated MIs per year worldwide, three million are STEMI. MI remains an early and long-term life-threatening condition.

The long-term efficacy and safety of clopidogrel has been established through landmark clinical trials in 100,000 patients and with clinical experience in 41 million patients treated worldwide since its launch.

Clopidogrel has demonstrated early and long term protection of the thrombotic patient in multiple trials: unstable angina and NSTEMI (CURE), thrombosis including recent MI, recent ischemic stroke, or symptomatic peripheral artery disease (CAPRIE).

Based upon these new clinical data sanofi-aventis and Bristol-Myers Squibb plan to meet with health authorities and discuss these study results and their support for an indication.

The CLARITY – TIMI 28 and COMMIT/CCS 2 trials were supported by grants from sanofi-aventis and Bristol-Myers Squibb.

Clopidogrel is marketed worldwide by sanofi-aventis (Paris Bourse: EURONEXT: SAN; New York: NYSE : SNY) and Bristol-Myers Squibb Company (NYSE: BMY) as Plavix® and Iscover®.