Prasugrel versus clopidogrel for ACS patients managed without revascularisation

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The first trial to study the effect of platelet inhibition in patients with acute coronary syndromes managed medically without revascularisation has found no significant difference between prasugrel and clopidogrel in the prevention of death, myocardial infarction or stroke.

The findings, from the phase III Targeted Platelet Inhibition to Clarify the Optimal Strategy to Medically Manage Acute Coronary Syndromes (TRILOGY ACS) study, were presented today at a Hot Line session of ESC Congress 2012 in Munich.

TRILOGY ACS was double-blind, randomised trial in which the effect of prasugrel (10 mg daily) was compared with that of clopidogrel (75 mg daily) for up to 30 months of treatment in ACS patients under 75 years with unstable angina or non-ST elevation myocardial infarction (non-STEMI) managed without revascularisation. All study subjects, who totaled 7243 in number, were taking aspirin, and the prasugrel dose was reduced to 5 mg daily for patients weighing less than 60 kilograms. The primary end point of the trial was cardiovascular death, myocardial infarction, or stroke. The study was performed at 966 sites in 52 countries.

Results showed that, through a median follow-up period of 17 months, the primary end point among participants under 75 years occurred in 13.9% of those treated with prasugrel and 16.0% of those treated with clopidogrel (HR 0.91; 95% CI 0.79-1.05; P=0.21). Similar results were observed in the overall patient population of 9326 patients, who included

an additional 2083 patients aged 75 years or older in whom a reduced dose of prasugrel (5 mg daily) vs. clopidogrel (75 mg daily) was explored.

However, an unexpected, time-dependent treatment effect was observed with a trend for a lower risk of ischaemic events with prasugrel after 12 months among patients under 75 years of age. Furthermore, a pre-specified analysis which accounted for all multiple recurrent ischaemic events (not just the first event among all components of the primary end point) suggested a lower risk with prasugrel (HR 0.85; 95% CI 0.72-1.00; P=0.044).

The rates of major, life-threatening, fatal and intracranial bleeding were infrequent and similar in each treatment group, both in patients over 75 years and in the overall population. The frequency of non-haemorrhagic serious adverse events was also similar by treatment, except for a higher frequency of heart failure in the clopidogrel group.

As background to the study, the study's chairman, Professor E Magnus Ohman from Duke University Medical Center, Durham, USA, explained that the patient population of the TRILOGY ACS trial has not been exclusively studied before in a randomised trial. Around 60% of ACS patients undergo revascularisation, but the remaining 40% are managed solely with drug therapy. "Patients who are medically managed are at higher risk for repeated cardiovascular-related events," said Professor Ohman. "So optimising medical therapy for these patients is extremely important."

The efficacy and safety of prasugrel and clopidogrel were first compared in the TRITON study of 2007 in ACS patients scheduled for PCI. This study found that prasugrel was associated with significantly lower rates of ischaemic events, including stent thrombosis, but with an increased risk of major bleeding. TRILOGY ACS, said Professor Ohman, was

designed as a follow-up to the TRITON trial, "to see if prasugrel was just as effective in ACS patients who aren't getting coronary stents or coronary bypass surgery".

The TRILOGY ACS study did not find an increase in severe bleeding complications with prasugrel as seen in the TRITON study, albeit with modification of the prasugrel dose for low-body weight (weight