

Focus on PLATO study

Roxana SISU, MD; Nora TOMA, MD

Cardiology Department, Emergency University Hospital, Bucharest, Romania

In Hot Line I Session of the ESC Barcelona 2009 the data from an important study in the field of acute coronary syndrome (ACS) were communicated: the PLATO study (Platelet Inhibition and Patient Outcomes) – Ticagrelor versus Clopidogrel in patients with ACS. In the same time, this study was published at NEJM.org. Ticagrelor is a reversible and direct-acting oral antagonist of the adenosine diphosphate receptor P2Y₁₂, that has a more rapid onset and more pronounced platelet inhibition than clopidogrel.

The PLATO study was a multicenter, randomized, double blind trial. It compared ticagrelor (180-mg loading dose, 90 mg twice daily thereafter) and clopidogrel (300-to-600-mg loading dose, 75 mg daily thereafter) for the prevention of cardiovascular events in 18,624 patients admitted to the hospital with an ACS, with or without ST-segment elevation, with an onset of symptoms during the previous 24 hours.

All patients received aspirin at a dose of 75 to 100 mg daily unless they could not tolerate the drug. For those who had not previously been receiving aspirin, 325 mg was the preferred loading dose; 325 mg was also permitted as the daily dose for 6 months after stent placement.

Outpatient visits were scheduled at 1, 3, 6, 9, and 12 months, with a safety follow-up visit 1 month after the end of treatment.

At 12 months, the primary end point, a composite of death from vascular causes, myo-

cardial infarction, or stroke, occurred significantly less often in the ticagrelor group than in the clopidogrel group (9.8% vs. 11.7%, $P < 0.001$). The difference in treatment effect was apparent within the first 30 days of therapy and persisted throughout the study period.

The secondary end points showed significant reductions in the ticagrelor group, as compared with the clopidogrel group, with respect to the rates of the composite end point of death from any cause, myocardial infarction, or stroke (10.2% vs. 12.3%, $P < 0.001$); the composite end point of death from vascular causes, myocardial infarction, stroke, severe recurrent ischemia, recurrent ischemia, transient ischemic attack, or other arterial thrombotic events (14.6% vs. 16.7%, $P < 0.001$); myocardial infarction alone (5.8% vs. 6.9%, $P = 0.005$); and death due to vascular causes (4.0% vs. 5.1%, $P = 0.001$).

There was also a reduction in the rate of death from any cause with ticagrelor (4.5%, vs. 5.9% with clopidogrel; $P < 0.001$). The rate of stroke did not differ significantly between the 2 treatment groups, although there were more hemorrhagic strokes with ticagrelor than with clopidogrel.

Among patients who received a stent during the study, the rate of stent thrombosis was lower in the ticagrelor group than in the clopidogrel group (1.3% vs. 1.9%, $P = 0.009$).

The ticagrelor and clopidogrel groups did not differ significantly with regard to the rates

Address for correspondence:

Roxana SisU, MD, Emergency University Hospital, Cardiology Department, 169 Splaiul Independentei, Zip Code 050098, Bucharest, Romania

email address: roxanel_sisu@yahoo.com

of major bleeding. With ticagrelor there were more episodes of intracranial bleeding (0.3% vs. 0.2%, $P = 0.06$), including fatal intracranial bleeding (0.1% vs. 0.01%, $P = 0.02$).

At Holter monitoring there was a higher incidence of ventricular pauses in the first week, but not at 1 month follow up visit, in the ticagrelor group. Pauses were rarely associated with symptoms and the 2 groups did not differ significantly with respect to the incidence of syncope or the necessity of pacemaker implantation.

In conclusion, the PLATO study showed that in patients who have an ACS with or without ST-segment elevation, treatment with ticagrelor as compared with clopidogrel significantly reduced the rate of death from vascular causes, myocardial infarction, or stroke without an increase in the rate of overall major bleeding but with an increase in the rate of intracranial bleeding. IT IS FOR THE FIRST TIME THAT INCREASING EFFICACY IN ANTITHROMBOTIC THERAPY IS NOT FOLLOWED BY AN OVERALL INCREASE IN BLEEDING RISK. □



Reference

Lars W, RC Becker, A Budaj et al, for the PLATO Investigators – Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes, *N Engl J Med* 2009; 361:1045-1057