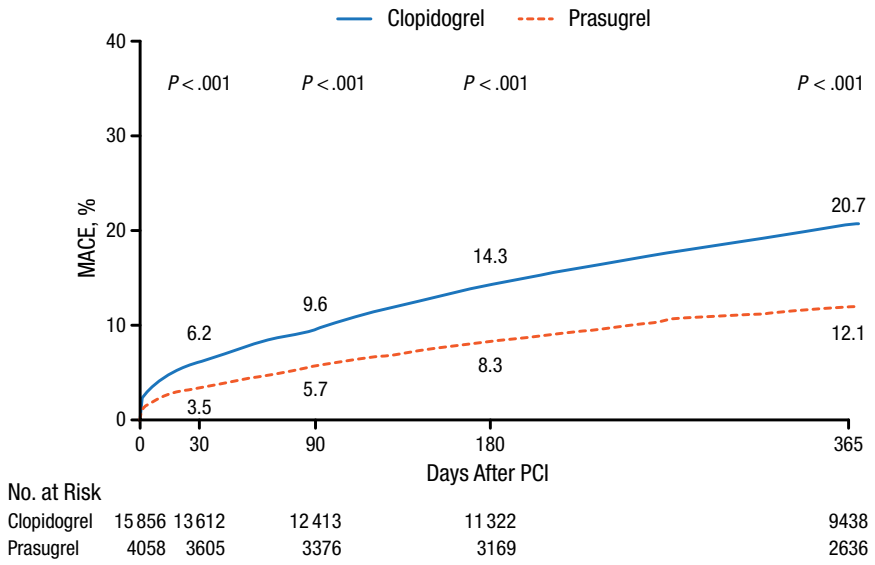
Figure 1. Unadjusted MACE Rates Over 1 Year in PROMETHEUS



MACE, major adverse cardiac event; PCI, percutaneous coronary intervention.
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Multivessel disease was identified in 41.2% of prasugrel-treated patients and 42.4% of clopidogrel-treated patients. In the prasugrel-treated group vs the clopidogrel-treated group, the stents were longer (31.4 vs 30.5 mm), larger in diameter (3.01 vs 2.96 mm), and more commonly a second-generation drug-eluting stent (81.2% vs 66.4%; $P<.05$ for all). The clopidogrel-treated vs the prasugrel-treated patients were more likely to receive periprocedural bivalirudin (74.0% vs 67.6%) and less likely to receive a glycoprotein 2b/3A inhibitor (21.4% vs 29.0%; $P<.05$ for all).

The primary efficacy end point of PROMETHEUS was the rate of major adverse cardiac events (MACEs; composite of all-cause death, myocardial infarction, stroke, and unplanned revascularization) at 90 days after the index PCI. The primary safety end point was bleeding that required hospitalization.

The unadjusted MACE rates showed a significant reduction with prasugrel vs clopidogrel (Figure 1), including for the primary efficacy end point at 90 days ($P<.001$).

Although the unadjusted hazard ratios (HRs) for MACE favored prasugrel at each assessment, the adjusted HRs were less significant. At 90 days, the unadjusted HR for MACE was 0.58 ($P<.001$), and the adjusted HR was 0.89 ($P=.17$). For myocardial infarction, the unadjusted HR was 0.51 ($P<.001$), but the adjusted HR was 0.84 ($P=.18$). For all-cause death at 90 days, the unadjusted HR was 0.21 ($P<.001$) and remained significant when adjusted (0.62; $P=.04$).

The unadjusted HRs for bleeding were significantly lower with prasugrel vs clopidogrel at each assessment, but the adjusted HRs showed no difference between the 2 treatments. At 90 days, the unadjusted HR was 0.65 ($P<.001$), and the adjusted HR was 1.03 ($P=.79$).

Dr Baber concluded that the lack of a difference in the bleeding rates with the 2 drugs after adjustment may reflect the selection of patients for PCI who are at very low risk for hemorrhagic complications. A possible interpretation of these data, he stated, is that the use of prasugrel should be based on the patient's risk for an ischemic event to achieve more benefit with the drug, and its broader use in eligible patients may yield results similar to those in clinical trials.

Ticagrelor Reduces Platelet Reactivity in Troponin Negative Patients With ACS Undergoing Non-Urgent PCI

Written by Emma Hitt Nichols, PhD

Ticagrelor treatment resulted in rapid and profound reduction in platelet reactivity compared with clopidogrel in low-risk troponin-negative patients with acute

coronary syndromes (ACS) who are undergoing elective or non-urgent ad hoc percutaneous coronary intervention (PCI). Roxana Mehran, MD, Mount Sinai Hospital, New York, New York, USA, presented data from an ad hoc PCI study in ACS patients [NCT01603082].

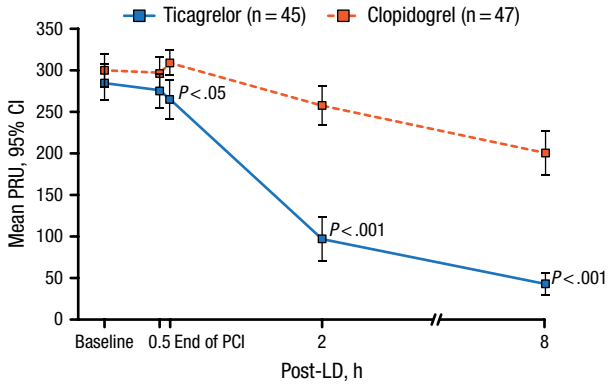
Ticagrelor is a potent $P2Y_{12}$-receptor inhibitor that is currently approved by the FDA for the treatment of patients with ACS. However, patients with low-risk ACS who are troponin-negative and undergo elective or non-urgent PCI may not receive a loading dose of a $P2Y_{12}$ receptor inhibitor prior to catheterization. The purpose of this study was to evaluate the effect of ticagrelor on platelet reactivity in patients with troponin-negative ACS undergoing ad hoc PCI who receive a loading dose in the catheterization laboratory immediately prior to PCI.

In this prospective, open-label, multicenter, phase 4 trial, 100 patients were randomly assigned to receive ticagrelor or clopidogrel. Patients in the ticagrelor arm (n = 51) received a 180-mg loading dose after diagnostic angiography followed by 90 mg 12 hours later. Patients in the clopidogrel arm (n = 49) received a 600-mg loading dose after diagnostic angiography. All patients received a 160- to 500-mg loading dose of aspirin followed by 75 to 100 mg of aspirin daily. Patients with ACS and ≥ 1 negative troponin test 6 to 48 hours after symptom onset were included in the study. Patients who used thienopyridine or ticagrelor within 7 days of randomization, had an indication for chronic anticoagulation, or concomitant therapy with a strong CYP3A inhibitor, substrates, or inducers were excluded.

The primary end point was platelet reactivity 2 hours after dosing of the study drug, which was measured by $P2Y_{12}$ reaction unit (PRU) level by the VerifyNow system. Secondary end points included PRU levels at 30 min after dosing, end of PCI, and 8 hours after dosing; percent reduction from baseline in PRU levels; and percent inhibition of platelet aggregation from baseline.

Patients who received ticagrelor demonstrated a significantly lower mean PRU level 2 hours after their loading dose compared with patients who received clopidogrel (treatment difference, −159.1; 95% CI, −194.7 to −123.5; $P < .001$). The significant difference in mean PRU levels occurred at the end of PCI and continued up to 8 hours following the loading dose of ticagrelor ($P < .001$; Figure 1). In addition, there was a significantly greater decrease in the reduction of PRU from baseline beginning at 2 hours after the loading dose compared with clopidogrel over the 8 hours ($P < .001$). Furthermore, inhibition of platelet aggregation was significantly greater in the ticagrelor arm compared with the clopidogrel arm across all time points.

Figure 1. Mean PRU Level After Treatment With Ticagrelor



LD, loading dose; PCI, percutaneous coronary intervention; PRU, platelet reaction units.
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The most common adverse events included chest pain, unstable angina, hypotension, dyspnea, and hematoma. Bleeding occurred in 5.9% of patients in the ticagrelor arm and 0 in the clopidogrel arm and all events were considered to be mild.

In conclusion, Dr Mehran stated that the data from this trial suggest that low-risk patients with troponin-negative ACS undergoing ad hoc PCI experienced greater platelet reactivity with ticagrelor treatment compared with clopidogrel.

ORBIT II: Orbital Atherectomy System Safe and Effective for Calcified Lesion Treatment

Written by Alla Zarifyan

Jeffrey W. Chambers, MD, Metropolitan Heart and Vascular Institute, Mercy Hospital, Minneapolis, Minnesota, USA, presented 2-year results of the ORBIT II study [Généreux P et al. *Am J Cardiol.* 2015], demonstrating that a coronary orbital atherectomy system (OAS) can be used as a lesion preparation tool prior to stent implantation in patients with severely calcified coronary lesions, and also had potential cost-saving benefits over standard treatment.

The prevalence of risk factors for arterial calcification (eg, advanced age, diabetes, and kidney disease) is increasing rapidly in the United States. Coronary calcium is a predictor of adverse outcomes in patients undergoing percutaneous coronary intervention for acute coronary syndromes [Généreux P et al. *J Am Coll Cardiol.* 2014]. Diamondback 360 is the first novel coronary OAS technology approved by the FDA to specifically treat