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].

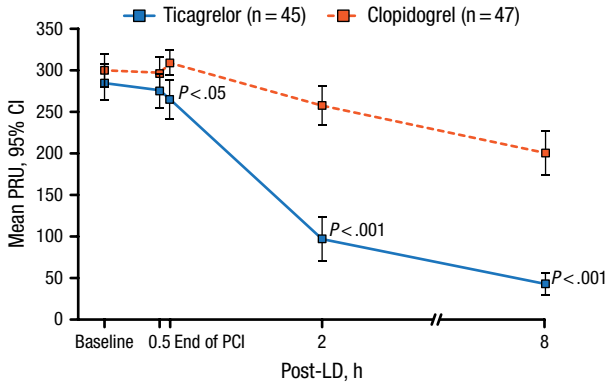
Ticagrelor is a potent $P2Y_{12}$-receptor inhibitor that is currently approved by the FDA for the treatment of patients with ACS. However, patients with low-risk ACS who are troponin-negative and undergo elective or non-urgent PCI may not receive a loading dose of a $P2Y_{12}$ receptor inhibitor prior 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

severely calcified lesions. It utilizes centrifugal sanding action, and Dr Chambers specifically highlighted its simplicity of use.

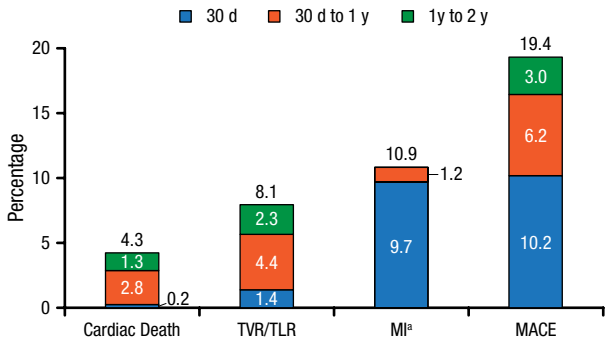
ORBIT II [Généreux P et al. *Am J Cardiol*. 2015] was a prospective, multicenter, nonblinded, single-arm study that evaluated the long-term safety and efficacy of coronary OAS in patients with severely calcified coronary lesions who underwent percutaneous coronary intervention. The objective of the study was to determine whether OAS successfully facilitated stent deployment and was safe in this patient population. The major inclusion criteria were evidence of severe calcification and the target vessel reference diameter between 2.5 mm and 4.0 mm, with the lesion length ≤ 40 mm.

The study enrolled 443 patients (64.6% men; mean age 71.4 years), with 97.7% of patients obtaining successful stent delivery that resulted in 98.6% of patients having < 50% residual stenosis [Chambers JW et al. *JACC Cardiovasc Interv*. 2014]. The adjudicated safety analysis showed that at 2-year follow-up, cardiac death occurred in 4.3% of patients, target vessel revascularization (TVR)/ target lesion revascularization (TLR) in 8.1% (TLR, 6.2%; TVR, 2.9%), myocardial infarction in 10.9%, and the composite end point of major adverse cardiac events in 19.4% (Figure 1). The subanalysis of the diabetic population revealed that coronary OAS produced similar outcomes in patients with diabetes (n = 160) vs those without (n = 283) at 2-year follow-up, with major adverse cardiac events occurring in 20.6% vs 18.7%, respectively.

The economic analysis compared OAS in elderly patients in the ORBIT II study (> 64 years; n = 297) with standard treatment in Medicare patients (n = 308) from hospitals reporting more than 10% of stent patients with calcification during the same time period. The baseline characteristics were comparable between these patient populations. The cost-model framework analysis revealed that the average projected cost offsets in the first year would fully cover the cost of OAS at $3795 and possibly extend to an additional $1118 in savings, yielding a total of $4913 in potential cost offset at 1 year. The incremental cost-effectiveness ratio (ICER) analysis demonstrated that OAS offered good value, with an ICER of $11 895 per life-year gained, which was substantially below the "high value" threshold of $50 000 per quality-adjusted life-year.

Dr Chambers concluded that the ORBIT II study showed that coronary OAS is a safe and effective treatment option in complex patients with calcified coronary lesions that is also cost-effective and potentially cost saving.

Figure 1. ORBIT II Safety Outcomes at 2-Year Follow-up



CEC, Clinical Events Classification; MACE, major adverse cardiac event; MI, myocardial infarction; TVR/TLR, target vessel revascularization/target lesion revascularization.

[a]Not per protocol analysis. Clinically driven evaluation based on CEC adjudication of MI.

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MILLION Study: Aggressive Medical Regimens Can Reduce BP and Lipids

Written by Emma Hitt Nichols, PhD

An aggressive, simultaneous amlodipine- and statin-based regimen significantly decreased blood pressure (BP) and low-density lipoprotein cholesterol (LDL-C) compared with a standard-intensity regimen in a Japanese population with coronary artery disease (CAD). Masa-aki Kawashiri, MD, Kanazawa University, Kanazawa, Japan, presented these unpublished data from the MILLION study.

Intensive statin therapy for lowering LDL-C had been demonstrated to reduce the risk of major adverse cardiovascular events compared with moderate-intensity statin therapy. In addition, lowering BP with an amlodipine-based regimen also reduced major adverse cardiovascular events in patients with hypertension compared with a β-blocker or angiotensin-converting enzyme inhibitor–based regimen. However, the combination of both LDL-C and BP lowering did not affect outcomes compared with standard therapy [Kohro T et al. *Circ J*. 2011]. The purpose of the MILLION trial was to evaluate the change in plaque volume using intravascular ultrasonography, BP, and lipids in a Japanese population with CAD.

In the open-label, multicenter MILLION study, 100 patients with CAD who underwent percutaneous coronary intervention were randomly assigned to receive standard therapy with amlodipine 2.5 mg and atorvastatin 5 mg and other agents as necessary to reduce BP to < 140/90 mm Hg and LDL-C to < 100 mg/dL, or aggressive treatment with amlodipine 5 mg and atorvastatin 10 mg and other agents to decrease BP to < 120/70 mm Hg