burden, with the majority of lesions comprising thin-cap fibroatheromas. In his concluding remarks, he also emphasized that although high-dose rosuvastatin therapy for 13 months is associated with a significant reduction of coronary atherosclerosis, it did not change the proportion of necrotic core in these arteries or the plaque phenotypes.

## NO Fails to Reduce Myocardial IS: NOMI Results

Written by Emma Hitt Nichols, PhD

Inhaled nitric oxide (NO) did not reduce infarct size (IS) in patients who experienced STEMI and underwent percutaneous coronary intervention (PCI). Stefan P. Janssens, MD, PhD, University of Leuven, Leuven, Belgium, presented data from the Effects of Nitric Oxide for Inhalation in Myocardial Infarction Size study [NOMI; NCT01398384].

In animal models, inhalation of 40 to 80 ppm of NO decreased IS and area at risk and improved functional recovery [Liu X et al. *J Am Coll Cardiol.* 2007; Hataishi R et al. *Am J Physiol Heart Circ Physiol.* 2006]. The hypothesis of the NOMI study was that inhaled NO would decrease IS and improve left ventricular (LV) function in patients with STEMI who underwent primary PCI.

The NOMI trial was a multicenter double-blind phase 2 trial that randomized 248 patients with STEMI undergoing PCI within 12 hours to either inhaled NO (80 ppm) or placebo. All patients underwent magnetic resonance imaging to evaluate IS, LV function, and remodeling at 48 to 72 hours and again at 4 months. The primary end point was IS and secondary end points included myocardial salvage index, myocardial hemorrhage, LV remodeling at 48 to 72 hours, and LV remodeling at 4 months. The trial also examined the effects on prespecified subgroups, including TIMI flow grade, culprit artery, time between symptom onset and PCI, and troponin levels upon admission.

Inhaled NO failed to significantly reduce IS, and the IS/LV mass ratio was 19.4% in the control arm and 18% in the inhaled NO arm (estimate R effect, –1.48; 95% CI, –5.25 to 2.29; $P=.44$). There were no differences in the composite end point of death, recurrent ischemia, stroke, and rehospitalization at 150 days (log-rank $P=.1022$). NO treatment resulted in a significant improvement in LV remodeling at 4 months (OR, 0.90; 95% CI, 0.81 to 0.999; $P=.048$) compared with control. There were no significant differences in the other secondary end points.

Prof Janssens stated that the data from the NOMI trial show that inhaled NO is safe but did not decrease the IS, as measured by percentage LV mass. However, there were improvements in LV remodeling at 4 months.

## TRO40303 Lacks Protective Effect in PCI: Results From MITOCARE

Written by Emma Hitt Nichols, PhD

TRO40303 failed to prevent reperfusion injury as measured by creatine kinase and troponin I levels in patients with STEMI when administered just prior to balloon inflation during percutaneous coronary intervention (PCI). Dan Atar, MD, Oslo University Hospital Ulleval, Oslo, Norway, presented data from the Safety and Efficacy Study of TRO40303 for Reduction of Reperfusion Injury in Patients Undergoing Percutaneous Coronary Intervention for Acute Myocardial Infarction [MITOCARE; Atar D et al. *Eur Heart J.* 2014].

TRO40303 blocks the opening of the mitochondrial permeability transition pore and was thought to prevent reperfusion injury. In animal models, TRO40303 reduced infarct size by 50% [Le Lamer S et al. *J Transl Med.* 2013] and improved left ventricular ejection fraction (LVEF) at 24 hours and 1 month [Augeul L et al. ESC 2009 (poster P4491)]. The purpose of the MITOCARE study was to determine the efficacy and safety of TRO40303 when administered prior to balloon inflation during PCI.

In this multicenter phase 2a trial, 167 patients with STEMI were randomized to either TRO40303 or placebo prior to PCI. The baseline characteristics were similar in both groups, although the TRO40303 arm had a higher mean age (64 vs 60 years) compared with the placebo arm. The mean time from the onset of pain to balloon time was 180 minutes, and the mean door-to-balloon time was 38 minutes.

The primary outcome of the study was infarct size as measured by area under the curve for creatine kinase and troponin I. The secondary outcome was infarct size as measured by magnetic resonance imaging. Patients were eligible for the study if they had no prior STEMI, presented with chest pain within 6 hours, and were to be treated with primary PCI, and there was TIMI 0/1 flow in the culprit artery. Patients were excluded if they had experienced cardiac arrest, ventricular fibrillation, cardiogenic shock, previous coronary artery bypass graft, or atrial fibrillation or they had a pacemaker.

There were no significant differences in creatine kinase ($P=.98$) or troponin I ($P=.57$) levels between the TRO40303 and placebo groups at 72 hours (Figure 1). In addition, the secondary end points—including myocardial salvage index, infarct size, microvascular obstruction, left ventricular end diastolic volume and end systolic volume, and LVEF—were similar between arms.