is injected via a catheter in the infarct-related artery following PCI. It penetrates through the damaged capillaries into the damaged heart tissue, where it settles and turns into a gel that acts like a 3-dimensional scaffold and prevents thinning of the left ventricular wall. After about 6 weeks, BL-1040 is reabsorbed and excreted through the kidney.

To be eligible for the study, subjects were required to be aged between 18 and 75 years, have experienced a first AMI (with 4 of 16 akinetic segments) with successful revascularization with PCI within 7 days, and have 1 or more of the following: left ventricular ejection fraction (LVEF) >20% and <45%; peak creatine kinase >2000 IU; and infarct size >25%, as measured by MRI. The primary study outcomes included adverse events (ie, MI, ventricular arrhythmias, cardiovascular hospitalization, symptomatic heart failure, renal failure, stroke, and death). Secondary outcome measures were: change from baseline in LV dimensions, regional (infarct-related) dimensions, global wall motion score, and LVEF. Follow-up visits occurred at 30, 60, 90, and 180 days post-procedure. Of the 10 subjects who have been treated to date, 4 have completed the 6-month follow-up period and 1 patient has completed the 3-month follow-up visit. Five patients have been recruited since January 2009.

At 90 days, LVEF increased to 49% (vs 47% at baseline). Diastolic volume decreased from 132 ml to 122 ml, and LV diastolic volume decreased from 67 ml to 62 ml. Pro-brain natriuretic peptide (BNP) levels went from 830 pg/ml to 480 pg/ml. No adverse events have been reported. The investigators have concluded that the use of BL-1010 is feasible and safe. Based on these early results, the ISMB unanimously approved opening enrollment to the remaining 25 patients. The study is expected to be completed in the third quarter of 2009.

Novel Interventional Approaches Are Effective Against Resistant Hypertension

Despite the availability of safe and effective pharmacological therapies, only about 50% of patients achieve adequate blood pressure control. Many patients develop resistant hypertension, which is characterized by an inability to achieve blood pressure targets despite multiple drug therapies at the highest tolerated dose. Patients with chronic uncontrolled hypertension are at high risk for major cardiovascular events, including early death, strokes, and renal disease.

At the American College of Cardiology 58th Annual Scientific Session, 2 late-breaking clinical trials evaluated novel nonpharmacologic options for the treatment of resistant hypertension.

Catheter-Based Renal Denervation

Disruption of the renal sympathetic nerves via catheter-based radiofrequency ablation markedly reduces blood pressure levels in patients with refractory hypertension, according to findings from a proof-of-concept study (NCT00483808).

The renal sympathetic nerves play a key role in the progression of hypertensive disease. A new catheter-based system uses radiofrequency ablation to disrupt renal sympathetic nerves without affecting other abdominal, pelvic, or lower extremity nerves. In this trial, the renal denervation system was evaluated in 45 patients with a mean baseline blood pressure of 177/101 mm Hg and a mean heart rate of 72 bpm. Five additional patients enrolled but did not undergo ablation due to complicated anatomical features.

Henry Krum, PhD, Monash University and Alfred Hospital, Melbourne, Australia, presented findings from the trial, which were simultaneously published online in *The Lancet.*

Among treated patients, mean blood pressure fell by 14/10 mm Hg within 1 month of the ablation procedure ($p<0.001$) and dropped by 27/17 mm Hg after 1 year ($p=0.02$). By comparison, blood pressure levels increased among the 5 patients who were enrolled but did not receive renal denervation. After 1 year, the mean blood pressure rose by 26/17 mm Hg.

Physicians were instructed not to alter treatment unless medically required, and so most patients remained on their antihypertensive drug regimen throughout the follow-up period. Three patients required reduction of their medications after their blood pressures normalized. Nine patients had their medications increased, including 5 patients who had blood pressure reductions of at least 10 mm Hg and 4 who did not respond to the procedure.

No major complications were observed in either the renal artery or the kidney, and there was no apparent effect

on renal function. The mean glomerular filtration rate (GFR) was 79 mL/min/1.73m^2 prior to the procedure and 83 mL/min/1.73m^2 6 months following renal denervation.

Percutaneous renal sympathetic denervation represents a simple and effective approach to the management of hypertension in patients who are refractory to conventional pharmacologic therapy, Dr. Krum concluded. Future trials will define the long-term efficacy of renal denervation in resistant hypertension and other disorders, he said.

Activation of the Carotid Baroreflex

An implantable device that activates the baroreceptors of the carotid sinus significantly reduces blood pressure in patients with refractory hypertension, according to results from a small phase 2 feasibility study.

In hypertensive patients, blood pressure receptors within the carotid sinus do not detect elevated intravascular blood pressure, leading to an inadequate autonomic response. The Rheos® hypertension system consists of a pulse generator, implanted near the collarbone, and carotid sinus leads. The device electrically stimulates the carotid sinus to activate blood pressure reflexes that lower heart rate, dilate blood vessels, and induce diuresis.

The phase 2 trial included 61 patients with systolic blood pressure ≥160 mm Hg who were resistant to 3 or more antihypertensive medications, including diuretics. After the Rheos device was surgically implanted and activated, blood pressure levels were measured at 1 year, 2 years, and 3 years. Marcos Rothstein, MD, Washington University School of Medicine, St. Louis, MO, presented findings in a late-breaking clinical trials session.

Mean blood pressure at baseline was 183/105 mm Hg despite treatment with a mean of 5.1 antihypertensive medications. On average, systolic blood pressure dropped by 25 mm Hg after 1 year, 22 mm Hg after 2 years, and 31 mm Hg after 3 years ($p<0.001$ at all time points). Diastolic blood pressure dropped by 15 mm Hg at 1 and 2 years and by 21 mm Hg by 3 years ($p<0.001$ at all time points).

Mean heart rate also fell by 7 bpm at 1 year ($p<0.005$), 8 bpm at 2 years ($p<0.005$), and 5 bpm at 3 years ($p=0.15$). Dr. Rothstein also observed a significant improvement in cardiac structure and function at 1 year, as measured by a decrease in left ventricular mass ($p<0.05$), left atrial dimension ($p<0.05$), and mitral A-wave velocity ($p<0.05$).

Based on promising early-phase results, the Rheos hypertension system is currently under evaluation in a phase 2 prospective, randomized, double-blind, placebo-controlled, multicenter trial with a target enrollment of 300 patients.

Clopidogrel Added to Aspirin Reduces Stroke Risk in Atrial Fibrillation Patients Unsuitable for Vitamin K Antagonist Therapy

For high-risk atrial fibrillation (AF) patients who are unsuitable for Vitamin K antagonist (eg, warfarin) therapy, dual antiplatelet therapy with clopidogrel and aspirin reduces the risk of major vascular events compared with aspirin alone, according to findings from the Atrial Fibrillation Clopidogrel Trial with Irbesartan for Prevention of Vascular Events (ACTIVE)-A trial (NCT000249873).

Stuart Connolly, MD, McMaster University, Hamilton, ON, Canada, reported findings from ACTIVE-A, which was designed to evaluate the addition of clopidogrel to aspirin in high-risk AF patients who were unsuitable for oral anticoagulation. A vitamin K antagonist, such as warfarin, is the treatment of choice for the prevention of stroke in high-risk patients with AF. However, due to increased bleeding risk, patient preference, or other medical contraindications, fewer than 50% of high-risk patients are suitable candidates for oral anticoagulation therapy.

ACTIVE-A included 7554 patients with documented AF, at least one risk factor for stroke, and no major risk factors for bleeding. All patients were treated with aspirin 75 to 100 mg/day, and were randomly assigned to additional treatment with clopidogrel 75 mg/day (n=3772) or placebo (n=3782). The primary outcome was a composite of major vascular events including stroke, myocardial infarction (MI), non-central nervous system (CNS) systemic embolism, or vascular death.

After a median follow-up of 3.6 years, dual antiplatelet therapy reduced the risk of the primary outcome by 11% compared with aspirin alone, from an annual rate of 7.6% to 6.8% (HR, 0.89; 95% CI, 0.81 to 0.98; p=0.01).

According to an analysis of the components of the primary endpoint, the benefit of clopidogrel was mainly in the reduction of stroke risk from 3.3% per year with aspirin alone to 2.4% per year with clopidogrel and aspirin