during the study (7% vs 25%; p<0.05), regardless of the severity of renal dysfunction.

Currently available potassium binders are poorly tolerated, with a high risk of severe gastrointestinal side effects. In the PEARL-HF study, RLY5016 was well tolerated, with a withdrawal rate that was comparable to that seen in the placebo group (7% vs 6%). More patients reported at least 1 adverse event in the RLY5016 group than in the placebo group (54% vs 31%; p=0.019), but they were mostly mild gastrointestinal side effects.

Three patients in the RLY5016 group developed hypokalemia, which may be prevented by lower doses of the phosphate binder, Prof. Pitt said. Future studies will evaluate whether lower doses of RLY5016 can prevent hyperkalemia among patients who are taking life-saving RAAS inhibitors for the treatment of HF, she concluded.

Elinogrel, a Reversible Platelet Inhibitor, Shows Promising Antiplatelet Activity in Nonurgent PCI

Elinogrel, an investigational $P2Y_{12}$ inhibitor, showed potent antiplatelet activity in the phase II Randomized, Double-Blind, Active Controlled Trial to Evaluate Intravenous and Oral PRT060128 (elinogrel), a Selective and Reversible $P2Y_{12}$ Receptor 0Inhibitor, versus Clopidogrel, as a Novel Antiplatelet Therapy in Patients Undergoing Nonurgent Percutaneous Coronary Interventions (INNOVATE PCI) trial. Compared with clopidogrel, elinogrel provided greater and more rapid platelet inhibition without increasing bleeding risk in patients who were undergoing elective percutaneous coronary intervention (PCI).

Stronger platelet inhibition has the potential to improve ischemic outcomes but often at the cost of increased major bleeding. Reversible platelet inhibition may lessen the risk of bleeding complications. Elinogrel is the only antiplatelet agent to competitively and reversibly bind the $P2Y_{12}$ receptor. The agent can be administered both intravenously and orally, enabling acute and long-term use.

In the INNOVATE PCI trial, 652 patients who were scheduled to undergo nonurgent PCI were randomly assigned to treatment with clopidogrel with an IV loading dose of 300 to 600 mg followed by 75 mg/day, or elinogrel with an IV loading dose of 80 mg followed by oral elinogrel 50 mg, 100 mg, or 150 mg twice daily. After study enrollment began, the protocol was adjusted to eliminate the elinogrel 50-mg dose and increase the elinogrel IV loading dose to 120 mg.

INNOVATE PCI was not powered for any specific endpoint but instead explored a range of efficacy, safety, and tolerability outcomes. Sunil Rao, MD, Duke University Medical Center, Durham, North Carolina, USA, reported findings from the INNOVATE PCI study.

Elinogrel provided a more rapid reduction in platelet aggregation compared with clopidogrel, with greater platelet inhibition at 30 minutes, 2 hours, and 20 hours after administration (p<0.025 for all comparisons). At 30 days, platelet inhibition remained greater with the elinogrel 100-mg and 150-mg oral doses compared with clopidogrel 75 mg.

There were no significant differences in ischemic event rates between the elinogrel and clopidogrel groups at 24 hours or 120 days, suggesting similar acute and chronic efficacy. Biological activity was also comparable, with similar degrees of troponin elevation in both treatment groups. Elinogrel did not increase the risk of TIMI major or minor bleeding compared with clopidogrel at either time point.

Dyspnea was more common with elinogrel 100 mg (15.4%) and elinogrel 150 mg (12.1%) compared with clopidogrel (4.3%), but most cases were mild and transient. Patients in the elinogrel 100-mg and 150-mg groups were more likely to develop elevated liver transaminases (2% and 3.4%, respectively) compared with clopidogrel (0.5%).

Following the promising results of INNOVATE PCI, a phase III trial of elinogrel in patients with chronic coronary heart disease will launch in early 2011. The trial will enroll approximately 24,000 patients with a history of myocardial infarction (MI). Patients will be randomized to low-dose or high-dose elinogrel or placebo. The primary efficacy endpoint will be cardiovascular death, MI, or stroke.

Management of ACS in Developing Countries: The ACCESS Registry

Results from the ACCESS Registry identified areas in which long-term ischemic events could be reduced in patients with acute coronary syndromes (ACS) in developing countries. Mohamed Sobhy, MD, FACC, Alexandria University, Alexandria, Egypt, discussed findings from the ACCESS registry.

The ACCESS Registry was a prospective, observational, multinational registry of patients who were hospitalized for ACS from January 2007 through January 2008 that was designed to evaluate the burden of ACS and patient outcomes in developing countries. It included 134 sites within 19 developing countries in Latin America, the Middle

East, North Africa, and South Africa. All patients (n=9732) were admitted within 24 hours of ischemic symptoms that were related to ACS and ECG changes, documented coronary artery disease, and/or elevated troponin/CK-MB concentration. Data were collected at baseline, discharge, 6 months postdischarge, and 12 months postdischarge. The primary endpoint was all-cause death, and secondary endpoints included cardiovascular (CV) death, CV death and nonfatal myocardial infarction (MI), nonfatal stroke, a composite of nonfatal MI, CV death, stroke, or MI, and rehospitalization for ischemic events, and bleeding episodes at 12 months postdischarge.

Fifty-two percent of the study population was diagnosed with non-ST-segment elevation (NSTE) ACS at discharge (24% NSTEMI and 28% unstable angina) compared with 45% that was diagnosed with ST-segment elevation MI (STEMI). The use of pharmacological therapies for ACS, such as aspirin, statins, β-blockers, and ACE inhibitors, was common for all study patients. Enoxaparin was used more frequently (57% for all ACS patients, NSTE ACS patients, and STEMI) than unfractionated heparin (40%, 37%, and 43%, respectively), while the use of other low-molecular-weight heparin and direct thrombin inhibitors as antithrombotic therapy was low. Coronary angiography was performed in 58% of all ACS patients, 59% of NSTE ACS patients, and 56% of STEMI patients versus percutaneous coronary intervention in 35%, 31%, and 40%, respectively. The rate of coronary artery bypass grafting was low in all groups (5.7%, 7.3%, and 3.8%, respectively). There was a low rate of reperfusion in the STEMI group (40%).

The rate of death at 12 months was highest among STEMI patients (8.4%) versus NSTE ACS (6.3%; $p<0.05$) and all ACS (7.3%). The most common cause of death was fatal MI (45% all ACS, 38% NSTE ACS, and 51% STEMI). The four strongest independent factors that were associated with 12-month death were cardiac arrest, cardiogenic shock, stroke/transient ischemic attack, and age >70 years. Higher rates of CV death, bleeding, and the combined composite endpoint were also observed in the STEMI group at 12 months.

These findings indicate that there is still work to be done to reduce the risk of long-term ischemic events in ACS patients in developing countries. Prof. Sobhy and colleagues were also able to identify independent factors that may predict disease mortality. These data can be used to develop solutions for ACS risk reduction in the developing world and highlight the unmet need to ease the escalating disease burden in these countries.