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n=1002) UFH, adjusted by blinded activated clotting time. The primary outcome was the composite of major bleeding, minor bleeding, or major vascular access site complications within 48 hours of PCI (Table 1). Key secondary outcomes included the composite of major bleeding within 48 hours of PCI with death, myocardial infarction (MI), or target vessel revascularization (TVR) within 30 days.

Table 1. Study Outcome Definitions.

Major Bleeding (OASIS 5)	• Fatal • Symptomatic ICH • Retroperitoneal hemorrhage • Intraocular bleeding leading to significant vision loss • Requiring surgical intervention • Hb drop of ≥3 g/dL • Blood transfusion of ≥ two units RBCs
Minor Bleeding	• Any other significant bleeding leading to transfusion of one unit of blood or discontinuation of antithrombotic therapy
Major Vascular Access Site Complications	• Large hematoma (≥5cm or requiring intervention • Pseudoaneurysm requiring treatment • Arteric-venous fistula • Other vascular surger related to the access site

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The rates that were associated with the composite primary outcome were similar for both UFH groups. Analysis of individual primary outcome components revealed similar rates between the two groups, with the exception of minor bleeds, which was lower in the low-dose UFH group (0.7% vs 1.7% in the standard group; p=0.04). The secondary composite outcome of peri-PCI major bleeding with death, MI, or TVR at 30 days favored the standard UFH regimen over low-dose UFH (3.9% for standard vs 5.8% for low-dose; OR, 1.51; 95% CI, 1.00 to 2.28; p=0.05). The rate of death, MI, or TVR at 30 days was also lower in the standard-dose group (2.9%) than in the low-dose group (4.5%; p=0.06). Catheter thrombus rates were low in both treatment groups (0.5% vs 0.1% in the standard-dose group).

The FUTURA/OASIS-8 results confirm the strength of current guidelines that recommend the standard-dose regimen of UFH during PCI. There was no significant difference in major bleeding or vascular complication between the two doses of UFH. The use of UFH in patients with ACS who are treated with FONDA who are undergoing PCI appears to be safe, but current UFH dose recommendations should be followed. It is important to note that patients who required urgent (<120 minutes) coronary angiography were excluded from participation in this study, which may have resulted in a lower-risk study population. Additionally, the study was not powered to fully compare the doses with regard to ischemic events alone, which influences the bleeding-versus-thrombotic risk assessment. Therefore, caution should be used when interpreting these data.

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New Potassium Binder Prevents Hyperkalemia in Patients with HF

An investigational potassium binder, RLY5016, prevented hyperkalemia in patients with heart failure (HF), according to findings from the phase II PEARL-HF study (NCT00868439). The new agent may allow more HF patients to use renin-aldosterone-angiotensin system (RAAS) blockers, which have been shown to reduce mortality but cause hyperkalemia in up to 25% of HF patients.

The PEARL-HF study included 104 patients with HF and either stage 3 or 4 chronic kidney disease or a history of hyperkalemia that resulted in RAAS inhibitor discontinuation. Patients were randomly assigned to treatment with RLY5016 30 mg/day (n=55) or placebo (n=49). The primary endpoint was the change from baseline in serum potassium by Week 4. Bertram Pitt, MD, University of Michigan School of Medicine, Ann Arbor, Michigan, USA, presented findings from the PEARL-HF study.

At baseline, all patients were receiving standard heart failure therapy with a RAAS inhibitor or β-blocker. Patients also received spironolactone 25 mg/day for the first 2 weeks of the study, and those with serum potassium levels ≤5.1 mEq/L on Day 15 increased the spironolactone dose to 50 mg/day. More RLY5016-treated patients than patients in the placebo group were able to increase the spironolactone dose for the remaining 2 weeks of treatment (91% vs 74%; p=0.019).

After 4 weeks, treatment with RLY5016 reduced mean serum potassium levels from 4.69 mEq/L at baseline to 4.48 mEq/L (mean change, -0.22 mEq/L). By comparison, potassium levels increased in the placebo group from 4.65 mEq/L to 4.93 mEq/L (mean change, +0.23 mEq/L), resulting in a between-group difference of 0.45 mEq/L that favored RLY5016 (p<0.001).

The new potassium binder also provided protection against hyperkalemia, which was defined as serum potassium ≥5.5 mEq/L. Fewer patients in the RLY5016 group than in the placebo group developed hyperkalemia at any point

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