rates of major bleeding was statistically significant—6.1% for upstream GPI vs. 4.9% for deferred GPI (p=0.009). Ischemic endpoints did not meet non-inferiority criteria (7.1% for upstream vs 7.9% for delayed). No difference in mortality was seen (1.3% upstream vs. 1.5% delayed) or MI (4.9% vs 5.0%), but unplanned revascularization for ischemia was slightly lower in the upstream group (2.1% vs 2.8%, p=0.03 for superiority). Among patients who went on to PCI (n=5,170), the composite ischemic endpoint was significantly lower in the upstream therapy group (8.0% vs 9.5%, p=0.05).

Among ACS patients, upstream GPI therapy was non-inferior for the net clinical benefit endpoint, compared with delayed GPI administration—but did not meet the criteria for non-inferiority for the ischemic endpoint.

Overall, ACUITY suggests that bivalirudin monotherapy reduces bleeding without a significant increase in events, compared with heparin + GPI. Meanwhile, ACUITY-Timing suggests that while upstream GPI is associated with fewer ischemic events, there was no difference in net clinical outcome between the two strategies.

"The bottom line is that bivalirudin monotherapy is as good as UFH or enoxaparin plus a IIb/IIIa blocker but with far less bleeding," said Dr. Stone. "Bivalirudin monotherapy will facilitate care tremendously."

However, session moderator Matthew Wolff, MD, Chief, Cardiovascular Medicine, University of Wisconsin, noted that ACUITY was a complex trial. "Results here become difficult to interpret," he said. "In ACUITY Timing, for example, only five hours separated the upstream and delayed use of GPI, which is not enough for meaningful comparison."

Dr. Wolff indicated that seeing all the data will be important. "Once the data is published we can assess various questions and caveats on dosages and timing this study raises."

REACH Registry

The REACH (Reduction of Atherothrombosis for Continued Health) study was specifically designed to determine the "real world" risk of a major adverse cardiac events (MACE) in patients with either established atherothrombotic disease or those who were at a high risk for this condition. It is the largest and most geographically extensive registry of its kind, with more than 68,000 patients in 44 countries, covering 6 regions and including 5,000 physician investigators. Patients were recruited based on a history of coronary artery disease (CAD), cerebrovascular disease (CVD) or peripheral vascular disease (PVD), or at least three risk factors for atherothrombosis, including diabetes, cigarette smoking, uncontrolled high blood pressure or uncontrolled high cholesterol levels at entry to study.

Patients with atherothrombotic disease, even in stable form, have a surprisingly high risk of death or major cardiovascular events, according to data from the registry. Within a year, one in eight patients will die, have a heart attack or stroke, or be hospitalized for a complication of vascular obstruction. The risk is even greater for patients with widespread disease burden.

At one year follow-up, investigators observed an overall MACE rate of 13%; noting that patients with peripheral arterial disease were at substantially higher risk, experiencing a one year MACE rate of 22%. In addition there was an incremental increase in risk in those with widespread atherothrombotic disease. In patients with atherothrombotic disease in one location only, the MACE rate was 13%, whereas in those with the disease in three locations, the MACE risk climbed to 28%.

"I find these event rates to be high, given that we are dealing with a stable outpatient population treated with contemporary therapy," said Dr. Gabriel Steg, professor of cardiology at Hôpital Bichat-Claude Bernard, Paris, on behalf of the REACH Reigstry's Scientific Council. "The REACH data shows that it is critical that we stop viewing atherothrombosis as a disease of a specific medical specialty – cardiology, neurology, or vascular disease – instead we must view it as a 'global' disease."