The Cardiovascular Research Foundation announces initiation of HORIZONS-AMI II Clinical Trial

March 27 2012

The Cardiovascular Research Foundation (CRF) today announced the initiation of the HORIZONS-AMI II randomized trial, evaluating Promus Element platinum-chromium everolimus-eluting stents versus Omega bare-metal stents in patients with heart attack undergoing primary angioplasty with bivalirudin anticoagulation. The HORIZONS-AMI II trial will also investigate the chronic use of the antiplatelet medications prasugrel versus clopidogrel in patients free of major events at 30 days.

The Harmonizing Outcomes with Revascularization and Stents in AMI II trial will enroll between 7,000 and 10,000 patients with ST-segment elevation myocardial infarction into two randomization arms, stent and pharmacology. The study will be powered for two primary endpoints at 12 months for the stent arm: to show 1) reduced death, myocardial infarction (MI) or target lesion revascularization, and 2) reduced stent thrombosis with the Promus Element stent compared to its bare-metal equivalent. In the pharmacology arm, the primary powered endpoint will be death, MI, stroke, definite/probable stent thrombosis, or TIMI major/minor bleeding between one and 15 months, designed to show similar outcomes between the two drugs.

Funded by the Boston Scientific Corporation and The Medicines Company, the HORIZONS-AMI II trial will be conducted in association with the Cardiovascular Research Foundation.

Data from the original HORIZONS-AMI clinical trial, completed in 2010, demonstrated that the administration of the anticoagulant medication bivalirudin during primary angioplasty increases survival and reduces bleeding compared to the use of heparin plus a glycoprotein (GP) IIb/IIIa inhibitor in heart attack patients. Use of a drug-eluting stent (paclitaxel) was also shown to be more effective than a bare-metal stent, with equivalent safety. Clinical data from the HORIZONS-AMI trial led to the recent FDA approval of Boston Scientific's Ion and Taxus Liberté drug-eluting stents to treat heart attack patients.

Since the HORIZONS-AMI trial was performed, newer, more effective, and safer stents have been introduced. The major safety concern with drug-eluting stents has always been stent thrombosis, the sudden development of a blood clot within the stent that can result in a heart attack or death. Promising data in moderate sized trials suggest that the polymer and drug combination used in the Promus Element stent (Boston Scientific) may be even safer than bare-metal stents. HORIZONS-AMI II will be the first adequately powered trial to test this hypothesis.

Moreover, since the first HORIZONS-AMI trial, antiplatelet agents more potent than clopidogrel, which is used for one year or more after stenting in patients with heart attack, have been introduced, including prasugrel (Effient, Daiichi Sankyo and Eli Lilly). The use of prasugrel rather than clopidogrel for up to 15 months clearly reduces the risk of second heart attack and stent thrombosis. However, most of this benefit is seen within the first 30 days; whether prasugrel is more effective than and as safe as clopidogrel after 30 days has not been specifically studied. This issue also has important cost implications as clopidogrel will become generic next year.

"The original HORIZONS-AMI trial established bivalirudin as an essential acute therapy to improve both early and late outcomes in

patients with heart attack, and demonstrated that Taxus drug-eluting stent use was safe," said lead investigator, Gregg W. Stone, MD, Professor of Medicine at Columbia University College of Physicians and Surgeons, and Director of Research and Education at the Center for Interventional Vascular Therapy at New York Presbyterian Hospital. Dr. Stone also serves as Co-Director, Medical Research & Education Division at the Cardiovascular Research Foundation.

"With HORIZONS-AMI II, we have the unprecedented opportunity to determine whether the Promus Element drug-eluting stent is actually not only more effective but also safer than bare-metal stents in heart attack patients, which would represent a true paradigm shift in interventional cardiology. Moreover, we will determine the safest and most effective anti-platelet agent to use in the chronic care of these high-risk patients," said Dr. Stone.

Provided by Cardiovascular Research Foundation