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CUTTING-EDGE STUDIES USHER NEW GENERATION OF HEART TREATMENT
*Studies on Mental Health, Individualized Dosing and Stents Using Stem Cells
Demonstrate Improved Understanding of Cardiac Damage and Mechanisms*

NEW ORLEANS, La. (March 24, 2007) — New technologies and recent discoveries have ushered in a new era of improved cardiovascular research, results of which are being presented today at the American College of Cardiology's 56th Annual Scientific Session. ACC.07 is the premier cardiovascular medical meeting, bringing together over 30,000 cardiologists to further breakthroughs in cardiovascular medicine.

This research demonstrates that the use of better technologies and improved understanding of cardiac mechanisms can help physicians more effectively treat heart conditions. One study demonstrates the clear link between clinical depression and heart failure outcomes, calling for better overall management of the disease. A second study shows early results from a stent that captures progenitor cells to accelerate the artery healing process, thereby reducing stent complications. A third study uses novel mechanisms to rapidly test patients for their response to anticoagulants, optimizing the dosage at which patients will respond best to the therapy.

"Cardiovascular disease is the leading cause of death today, and the major focus now is to find better ways to help these patients through prevention, intervention and long-term treatment," said Douglas P. Zipes, M.D., Distinguished Professor of the Indiana University School of Medicine.

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Depression Worsens Survival And Major Outcomes In Elderly Patients With Chronic Heart Failure: An Analysis Of 18,623 Patients In A Community Setting. (Presentation Number: 907-217)

Cardiovascular research has evolved over the years to incorporate formerly unknown risk factors and comorbidities, including important mental health factors. Previous studies have suggested a link between depression and poor survival rates in elderly patients with heart conditions, but have not addressed a large-scale population of hospitalized patients to assess the direct impact of the two factors. This study of nearly 20,000 elderly patients reviewed the prevalence and association of depression (D) with clinical outcomes among high-risk elderly heart failure (HF) patients, showing significant compromise of their health.

To gain an accurate assessment of the prevalence of depression in this population, the team selected a total of 18,623 patients older than 60 years from hospital records, prescription databases and vital statistics in Italy from January 2000 through December 2003. Of these, 2,405 (12.9%) were being treated for clinical depression with psychotropic drugs prior to their HF diagnosis, and were generally older than the overall participant pool, of female gender and more often presented a history of peripheral vascular disease and stroke. Heart failure in this case was defined as either chronic HF diagnosis at the hospital or chronic HF treatment (<45 days) with any combination of heart treatments, including ACE-inhibitors, digoxin, furosemide, carvedilol, spironolactone or ARB-blockers.

Among the selected population, patients treated for depression experienced significantly worsened major outcomes, including all-cause mortality (OR +28%), the composite of stroke, TIA (transient ischemic attack, or mild stroke) or AMI (acute myocardial infarction) (OR +36%) and rehospitalization for any reason (OR +18%), a surprisingly high-risk finding linking the two conditions. However, the patients with depression did not experience higher rates of rehospitalization for CHF (OR +0%) compared to the overall participant population.

"We have focused primarily on biological risks and known co-morbidities in elderly heart failure patients, but this trial demonstrates the critical importance of mental health monitoring for successful management of heart failure in this population," said Aldo Maggioni, M.D., of the

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ANMCO Research Center in Italy and co-author of the study. "Effective methods to monitor and treat depression in nursing homes should be implemented to improve the quality of life for patients with heart failure."

Dr. Maggioni will present this study on Sunday, March 25, at 3:00 p.m. in Hall H.

First Real World Experience and Six Months Clinical Outcome in Patients Treated with a Genous™ Endothelial Progenitor Cell Capturing Stent (Presentation Number: 907-211)

Stents have delivered much clinical progress as well as controversy over the past several years, as cardiologists search for better options to heal arteries in their patients. Drug-eluting stents have offered new options and better success rates, but still have problems with delayed healing and late thrombosis. A new trial presented today shows strong initial results with the use of a stent that attracts circulating progenitor cells to help create a functioning endothelial layer, essentially accelerating the artery healing process.

The Genous™ Endothelial Progenitor Cell (EPC)-capturing stent is coated with an antibody (CD34+) that attracts EPCs, causing them to differentiate into a functional endothelial tissue layer in the artery. Researchers predict the layer may help accelerate healing, thereby reducing in-stent restenosis and possibly preventing stent-related thrombosis. With the addition of statin therapy, which increases the number of EPCs in the peripheral blood, the process may be even more effective.

The single-center study treated 87 patients with coronary artery stenosis who were treated with statin therapy for at least two weeks prior to intervention, and achieved positive clinical outcomes during a six-month assessment. No participants died during the study, and TIMI 3 flow was achieved in 99.3 percent of all treated lesions. Only one side branch failure occurred, leading to an in-hospital MI, target vessel revascularization was required in three patients and one patient required a non-target vessel revascularization.

"Treatment of coronary artery stenosis with this EPC-attracting stent in statin-treated patients shows excellent procedural success so far," said Marcel Beijk, M.D., of the University of Amsterdam and lead author of the study. "While this is still an early study, it offers a whole new look at the use of stents and the process of healing damaged tissue throughout the body. As we

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look at new treatment combinations, we believe this is a step in the right direction to offer patients better long-term success rates."

Dr. Beijk will present this study on Sunday, March 25, at 8:30 a.m. in Room 245.

A Rapid Genotyping Assay for Polymorphisms Affecting the Dose-Response to Warfarin Therapy (Presentation Number: 1020-89)

The new generation of medicine is moving toward personalized care, where patients can be tested for their individual response to certain therapies, thereby improving the quality of care they receive and maximizing their chances for long-term survival. Early studies on genetic testing have been promising, but application of most of these tests to-date has been limited to certain high-risk needs. This study by researchers at Intermountain Healthcare and the University of Utah is the first trial to apply genetic testing in a same-day clinical trial setting to determine the best dosage of warfarin, a commonly used anticoagulant for heart patients.

There is known variability in patient response to warfarin, which is caused in part by variations in the CYP2C9 and VKORC1 genes. Previous studies have shown that patients carrying at least one of these variants are more sensitive than non-carriers to doses of warfarin, so FDA guidelines have recommended genotyping patients for these variants to determine the best individual doses to initiate and maintain therapy. This trial used a rapid (same-day, 1-hour) genotyping method to guide optimal warfarin dosing without delaying initiation of therapy.

The genotyping process was similar to standard practices, but the method abbreviated the analysis time to allow for rapid results. On average, the turn-around time for the results was 68 minutes. (Currently available commercial testing typically requires a one to several day turnaround time.) In this study, patient DNA was extracted and PCR (polymerase chain reaction) amplified it for the *VKORC1* and *CYP2C9**2 and *3 polymorphisms. Importantly, in addition to being rapid, the process was extremely accurate, as it was successfully validated by comparison with sequencing: the test found 100 percent concordance for *VKORC1* (N=140) and *CYP2C9**3 (N=96) variants, and 98 percent agreement for *CYP2C9**2 (n=51).

While the test remains to be researched in larger trial sets, the goal of the rapid testing method is to allow for same-visit application of genotyping to improve timeliness (same-visit

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initiation) of therapies whose doses are specific to genotype in both clinical trials and regular practice settings.

"We are excited to put this technology into practice and more accurately and *quickly* provide the right dose of warfarin to patients who need to manage their risk of thromboembolic events," said Jeffrey Anderson, M.D., of Intermountain Healthcare (LDS Hospital) and the University of Utah, and lead author of the study. "Ultimately, we hope genetic-driven dosing regimens will improve the efficiency and safety of anticoagulant therapy as well as extend to other areas of cardiovascular medicine."

Dr. Anderson will present this study on Monday, March 26, at 3:30 p.m. in Hall H.

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The American College of Cardiology (www.acc.org) represents the majority of board certified cardiovascular physicians in the United States. Its mission is to advocate for quality cardiovascular care through education, research, promotion, development and application of standards and guidelines- and to influence health care policy. ACC.07 and the i2 Summit is the largest cardiovascular meeting, bringing together cardiologists and cardiovascular specialists to share the newest discoveries in treatment and prevention, while helping the ACC achieve its mission to address and improve issues in cardiovascular medicine.