Late-Breaking Clinical Trial Abstracts From the American Heart Association’s Scientific Sessions 2006

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Late-Breaking Clinical Trial Abstracts

Late-Breaking Clinical Trials I

FAME (The First Clinical Study of Adherence to Medications in the Elderly): A Randomized Controlled Trial on the Impact of a Medication Adherence Program on Control of Lipids and Blood Pressure

Jeanie K Lee, Karen A Grace, Allen T Jay; Walter Reed Army Med Ctr, Washington, DC

Background: Elderly patients with coronary risk factors frequently require polypharmacy which places them at increased risk for medication nonadherence. Poor medication adherence is prevalent, difficult to manage, and diminishes the health benefits of pharmacotherapies. Effective strategies to improve adherence in the elderly are lacking, and improved health outcomes in this population have not been demonstrated. Methods: Community-based patients, ≥65 years old and taking ≥6 chronic medications per day were enrolled. After a 2-month run-in phase during which baseline adherence (via pill counts), blood pressure, and LDL-C were measured, participants entered a 6-month intervention phase consisting of standardized medication education by a clinical pharmacist and medications dispensed in daily, dose-specific blister packs. The primary endpoints were the change in medication adherence and the changes in LDL-C and blood pressure. Following the intervention phase, participants were randomized to combination pharmacy care blister packages versus usual care (pill bottles) for an additional six months followed to the primary endpoints of the difference in medication persistence in the 2 arms, and changes in LDL-C and blood pressure. Results: 200 pts (77.5% male), mean age 79 ± 8, taking a mean of 9 ± 3 chronic meds were studied. Coronary risk factors included treated hypertension in 92% and treated hyperlipidemia in 81%. Baseline medication adherence was 61.3 ± 13.6%. At six months, medication adherence increased to 96.7 ± 7.1% (P < 0.001) and was associated with significant improvements in systolic blood pressure (132.7 ± 14.6 to 129.0 ± 16.0 mm Hg; P = 0.005) and LDL-C (84.1 ± 25.9 to 96.9 ± 24.8 mg/dL; P = 0.003). The results of the randomized controlled trial studying the relationship between pharmacy care blister packages vs usual care on adherence and blood pressure/LDL-C will be presented (last follow-up August 2006). Conclusion: Among elderly patients at risk for medication non-adherence receiving polypharmacy for cardiovascular risk factors, a comprehensive pharmacy care program consisting of patient education and blister-packed medications increases medication adherence >50% and provides clinically-meaningful reductions in blood pressure and LDL-C.

Multinational Etoricoxib and Diclofenac Arthritis Long-Term (MEDAL) Study Program: Cardiovascular Outcomes Following Long-Term Treatment With Etoricoxib Versus Diclofenac in Patients With Osteoarthritis and Rheumatoid Arthritis

Christopher P Cannon, TIMI Study Group, Brigham & Women’s Hosp, Boston, MA; for the MEDAL Steering Committee

Introduction: The cardiovascular (CV) safety of traditional NSAIDs and COX-2 selective inhibitors is an issue of great clinical importance. We hypothesized that the risk of thrombotic CV events in arthritis patients receiving treatment with etoricoxib would be non-inferior to the risk associated with diclofenac treatment. Methods: The MEDAL Program consists of 3 randomized, double-blind trials that randomly assigned patients with osteoarthritis (N = 24,912) or rheumatoid arthritis (N = 7,985) to etoricoxib (60 or 90 mg daily) or diclofenac (150 mg daily). The primary endpoint was thrombotic CV events as confirmed by a blinded adjudication committee. Non-inferiority was defined as an upper 95% CI bound of the hazard ratio = 1.20. The primary endpoint was CV death, MI, stroke, or arterial thrombosis. Results: Total CV events were over 40,000 events in 12,000 events with 1 over 4 of these deaths annually. The hazard ratio was 0.85 (95% CI 0.75-0.96) for CV events. Conclusion: The MEDAL program is the first randomized trial assessing non-inferiority of CV risk with a COX-2 selective inhibitor versus a traditional NSAID.

Effects of Pioglitazone Compared to Glimepiride on Carotid Intima-Media Thickness (CIMT) in Type 2 Diabetes: Results of the CHICAGO Study

Theodore Mazzone, Univ of Illinois at Chicago, Chicago, IL; Peter M Meyer, Steven B. Feinstein, Rush Univ Med Ctr, Chicago, IL; Michael H Davidson, Radiant Rsch, Chicago, IL; Ralph D’Agostino, Boston Univ, Boston, MA; George T Kondos, Univ of Illinois at Chicago, Chicago, IL; Alfonso Perez, Takeda Global Rsch and Development, Lincolnshire, IL; Steven M Halfner; Univ of Texas Health Science Ctr, San Antonio, TX

Carotid artery intima-media thickness (CIMT) is independently predictive for risk of cardiovascular (CV) events, which are markedly increased in type 2 diabetes (T2DM). In a double-blind, multicenter, randomized study, we compared the effects of pioglitazone (PIO) to glimepiride (GLM) on CIMT progression over 16 months in 462 subjects from the racially diverse Chicago metropolitan area. CIMT images were taken by a single ultrasonographer and measured centrally using computerized edge-detection technology. The primary endpoint was posterior wall CIMT of the common carotid arteries at Final Visit. Mean age was 50 years, BMI 32 kg/m2, T2DM duration 7.7 years, A1c 7.4%, and BP 129/78 mmHg. At baseline, 70% of subjects had hypertension, 64% had hyperlipidemia, 55% had statin use, and 57% had ACE/ARB use. Mean CIMT was less with PIO compared to GLM at all assessments (Weeks 24, 48, 72). For the primary endpoint, progression of mean CIMT was less with PIO relative to GLM (0.091 mm vs. 0.012 mm, respectively; difference: -0.013 mm; 95% CI: -0.024, -0.002; P = 0.017). PIO also slowed progression of maximum CIMT compared to GLM (0.002 mm vs 0.026 mm, respectively; difference: -0.024 mm; 95% CI: -0.042, -0.006; P = 0.008). Fewer PIO (N = 8) than GLM (N = 14) subjects had adjudicated CV-related death, MIs, stroke, coronary revascularization, carotid endarterectomy/stenting, and hospitalization for unstable angina or CHF. At study end, glycemic control was similar between groups. Relative to GLM, PIO resulted in greater reduction of triglycerides (-15.6%, 95% CI: -23.8, -7.2), greater increase of HDLC (13.9%, 95% CI: 10.5, 17.3), and no difference in LDL-C (4.9%, 95% CI: -1.2, 10.6). Hypoglycemia was more common in those with GLM and edema and weight gain were more common with PIO. In an 18-month trial in T2DM subjects, PIO slowed progression of CIMT, a marker of coronary atherosclerosis and a risk predictor of MI and stroke, compared to GLM.

A Randomized Trial of Folic Acid and B-Vitamins in the Secondary Prevention of Cardiovascular Events in Women: Results From the Women’s Antioxidant and Folic Acid Cardiovascular Study (WAFACS)

Christine M Albert, Nancy R Cook, J M Gaziano, Elaine Zaharris, Jean MacFadyen, Eleanor Danielson, Julie E Buring, JoAnn E Manson; Div of Preventive Medicine, Brigham and Women’s Hosp, Boston, MA

Background: Recent secondary prevention randomized trials have failed to support benefits of folic acid in combination with B-vitamins on CVD risk. However, few women participated in these trials and concerns persist that background folic acid fortification in the food supply may have contributed to null findings. Objective: WAFACS tested a combination of folic acid (2.5 mg daily), vitamin B6 (50 mg daily), and vitamin B12 (1mg daily) compared to placebo on the primary outcome of MI, stroke, revascularization, or CVD death among women at increased risk of CVD. Methods: 5,442 female health professionals participating in a randomized trial of antioxidant vitamins were randomized to a combination of folic acid/vitamin B6/vitamin B12 or placebo. Participants were 40 years or older with a prior history of CVD or three or more CVD risk factors, and were followed for an average of 7.3 years. In a sub-study of 300 women, blood samples collected at study entry in 1993–1995 prior to initiation of folic acid fortification in 1998. Primary study completion in 2006 was analyzed for folic acid and homocysteine impacts. Results: 859 women experienced a CVD outcome, including 139 MIs, 148 strokes, 508 coronary revascularizations, and 200 CVD deaths. There was no overall effect of folic acid/vitamin B6/vitamin B12 on the primary combined endpoint (RR=1.01, 95% CI=0.91–1.19, p=0.58). There were no significant effects on the individual secondary outcomes of MI (RR=0.87, 95% CI=0.58–1.33, p=0.50), stroke (RR=1.14, 95% CI=0.82–1.57, p=0.44), revascularization (RR=0.99, 95% CI=0.83–1.17, p=0.87), or CVD death (RR=1.03, 95% CI=0.78–1.36, p=0.82). In the blood sub-study, active treatment significantly decreased homocysteine levels (geometric mean, 10.0 vs 12.5, P<0.001). In the placebo arm, folic acid levels increased geometric mean = 9.0 vs 18.4, P<0.001, secondary to background folic acid fortification in the food supply; however, this did not lower homocysteine levels. Conclusion: There was no overall effect of a combination of folic acid/vitamin B6/vitamin B12 on CVD events among women at high risk for CVD despite significant homocysteine lowering. Homocysteine lowering by background folic acid fortification in the food supply does not appear to account for these null findings
Effects of Percutaneous Revascularization of Occluded Infarct-Related Arteries on Left Ventricular Function and Late Vessel Patency: Results of the Total Occlusion Study of Canada-2, an Ancillary Study of the OAT Trial

Vladimir Dzavik, Toronto Gen Hosp, Toronto, Canada; Deborah Atkinson, Toronto General Hosp, Univ Health Network, Univ of Toronto, Toronto, Canada; Genell Knauff, Maryland Med Resch Institute, Baltimore, MD; John G Mancini, Vancouver General Hosp, Vancouver, Canada; Sandra Forman, Maryland Med Resch Institute, Baltimore, MD; John R Ross, Toronto General Hosp, Univ Health Network, Univ of Toronto, Toronto, Canada; Warren J Cantor, St. Michael’s Hosp, Toronto, Canada; Ronald J Careere, St. Paul’s Hosp, Vancouver, Canada; John P Gruenwald, Sileman Med Ctr, Katowice, Poland, Boban Mihailovic, Thomas Hosp, Fernando Fonseca, Amadora, Portugal; Eric A Cohen, Sunnybrook Health Sciences Ctr, Toronto, Canada; Anthony Ganz, Hotel Dieu Grace Hosp, Windsor, Canada; James M Rankin, Royal Perth Hosp, Perth, Australia; Gerald Devlin, Waikato Hosp, Hamilton, New Zealand; Carlos A Vozzi, Instituto De Intervenciones Cardiovasculares, Buenos Aires, Argentina; Anthony G Lim, Mount Sinai Med Ctr, Miami, FL; Judith S Hochman, New York Univ, New York, Canada; Christopher E Builer, Vancouver General Hosp, Vancouver, Canada; The Total Occlusion Study of Canada-2 (TOSCA-2) investigators

Background: The strategy of opening a persistently occluded infarct-related artery (IRA) beyond the acute phase of myocardial infarction (MI) remains unresolved. Small studies have shown mixed clinical results and no clear benefit in left ventricular function or remodeling. The Total Occlusion Study of Canada -2 (TOSCA-2) is a NHLBI-funded international randomized ancillary study of the Occluded Artery Trial (OAT) prospectively testing the effect of contemporary PCI on left ventricular (LV) function and long-term IRA patency in patients with persistent IRA occlusion. TOSCA-2 is designed to provide key mechanistic insights into the effect of the latest generation of clinical outcomes (TV: treated in the placebo or OAT). Methods: Patients with an occluded (TIMI grade 0 or 1) native IRA ≥3–28 days after MI were randomized to PCI with stenting of the IRA and optional medical therapy (PCI) or medical therapy alone (MED). TOSCA-2 patients consented to undergo repeat coronary and LV angiography 1 year, 3 months after randomization. Co-primary endpoints were change in LV ejection fraction (EF) and IRA patency by core laboratory analysis. Secondary endpoints included change in LV end-systolic and end-diastolic volume indices (ESVI, EDVI). The target sample size was 380 patients. Results: Between June 1, 2006, and July 2005, 301 of 2,169 patients (14%) randomized to OAT were enrolled in TOSCA-2, in 32 participating sites. Mean time from MI to randomization was 10 days in both groups. The PCI and MED groups were balanced in age (57.3 vs. 57.8 years), sex (16.9% vs. 17.7% women) LAD IRA (30.8 vs. 42.5%) and multi- vessel disease (18.5 vs. 12.1%) (all p~ns). There were fewer diabetics in the PCI group (16.4% vs. 25.3%, p=0.03). These characteristics were similar to those of the OAT population. Baseline angiographic measures were also balanced, including EF (48.2% vs. 47.5%), EDVI (67.5 vs. 66.1 ml/m2), EDVI (131.1 vs. 125.3 ml/m2) and TIMI grade 0 antegrade IRA flow (80 vs. 63%) (all p =ns). The interim 1-year angiographic follow-up rate is 85%. Conclusions: TOSCA-2 results provide a large and representative subset of the overall OAT population with well balanced baseline characteristics. The primary and secondary endpoints of TOSCA-2 will be presented.

Late-Breaking Clinical Trials II

Assessment of Pexelizumab in Acute Myocardial Infarction (APEX AMI): A Multicenter, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled Study of Pexelizumab in Patients With Acute Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention

Paul W Armstrong, Univ of Alberta, Edmonton, Canada; Peter X Adams, Alexion Pharmaceuticals Inc., Cheshire, CT; Christian W Hamm, Kerckhoff Heart Cntr, Bad Nauheim, Germany; William W O’Neill, Beaumont Heart Cntr, Royal Oak, MI; Alec S Vahanian, Hopital Bichat, Paris, France; Christopher B Granger, Duke Clinical Rsch Institute, Durham, NC; David R Holmes, Mayo Clinic, Rochester, MN; Thomas G Todorov, Procter & Gamble Health Care Rsch Ctr, Mason, OH; Frans Van de Wert; Univ Hosp Gasthuisberg, Leuven, Belgium

Hypothesis and Purpose: The primary objective of this study is to determine whether pexelizumab treatment reduces all-cause mortality at day 30 in patients with acute STEMI undergoing primary PCI. Secondary objectives are to determine whether pexelizumab treatment in patients with acute STEMI expected to undergo primary PCI reduces: (a) death through day 90; (b) composite endpoint of death, cardiacogenic shock or CHF through Day 30; Study Design and Methods: Multi-center, randomized, double-blind, parallel-group, placebo-controlled, phase 3 study of intravenous pexelizumab in conjunction with primary PCI. Patients were stratified by location of MI (high-risk inferior or other MI location) and randomized to either active treatment or placebo. Sample Size: 5,745 patients with last enrolled patient May 11, 2006. Intervention(s): Patients received 2 mg/kg IV bolus pexelizumab, a CS complement inhibitor, or placebo given over 10 minutes, followed as soon as possible by 0.05 mg/kg per hour infusion of pexelizumab or placebo over the next 24 hours. The entire bolus of study medication intended to be given before balloon inflation and/or stent placement. Power Calculations: Assuming a placebo Day 30 mortality rate of 4.6%, our sample size of 5,745 patients allows for adequate (80%) power to detect an approximate 30% reduction in Day 30 mortality. Meta-analysis of Day 30 mortality, incorporating all 5 prior pexelizumab randomized placebo-controlled ischemia/reperfusion trials (n=9,233) with the APEX trial, will provide additional context for the APEX results. Primary End Points: Death through day 30. Secondary End Points: Death through day 90, and composite endpoint of death, cardiacogenic shock or CHF through Day 30. Outcomes (Statistical Plan or Main Results): The primary statistical methodology for all the efficacy analyses will be based on intention-to-treat and on time-to-event analysis. The Kaplan-Meier (K-M) estimates of the survivor function, life table estimates of the survivor and hazard functions will be computed, and presented in graphical form in the placebo and pexelizumab groups. A simple Cox proportional hazards model will be used to obtain an estimate of the hazard ratio for the pexelizumab group to the placebo group. A 95% confidence interval will be computed for the hazard ratio.

The Outed Artery Trial (OAT)

Judith S Hochman, New York Univ Sch of Medicine, New York, NY; on behalf of the OAT Rsch Group

Background: Experimental and clinical evidence suggests that PCI late post-MI may benefit patients with persistent total occlusion of the infarct-related artery (IRA). However, prior small randomized trials have yielded conflicting results. Clinical practice at present reflects equipoise, with about half of clinicians treating patients with occluded IRAs with PCI, and the other half offering conservative therapy. Methods: OAT, an international study funded by NHLBI, tested the hypothesis that PCI with stenting, compared to medical therapy alone, would reduce by ≥25% the risk of death, recurrent MI or hospitalization/ treatment for NHYA class IV CHF in asymptomatic patients with total IRA occlusion 3 to 28 days post-MI day 1 – calendar day of symptom onset; minimum time MI onset to randomization: ≥ 25 hours. Patients with TIMI 0 or 1 flow in the IRA following MI (ST elevation or non ST elevation, Q wave or non-Q wave) were eligible if they were at high risk defined as EF ≤ 50% OR proximal IRA occlusion (LAD proximal to the second diagonal, large RCA or large dominant or co-dominant circumflex artery). Major exclusion criteria included significant proximal three-veesel or left main disease, rest angina, severe inducible ischemia or NYHA III–IV CHF. An independent committee adjudicated endpoints. Secondary endpoints include cardiac death, hospitalization for CHF, stroke and others. Results: As of 12/31/05, 2,186 patients were randomized in the main OAT trial. The average age was 67 years (58.6 ±11.1) and 74% were male (58% were women). IRAs were present in 23%, of MI in 11%, hypertension in 46% and diabetes in 21%. The IRA was the LAD in 36%, RCA in 49% and LCX in 15%. Fibriyolitic therapy had been administered in 19%. The mean EF was 49.3% ± 10.8. Patients were randomized a median of 6 days (IQR 5–18 days) after use of all evidence-based therapies was recommended. The mean follow up was 3 years. The rate of crossovers plus failed PCI was lower than the projected 25%. Conclusions: OAT is the first adequately-powered randomized study to test the late open artery hypothesis. The occurrence of primary and secondary endpoints will be presented. Given clinical equipoise as well as benefit of late opening of the IRA, the results should have a substantial impact on clinical practice.

Large-Scale Trial Using Atial Natriuretic Peptide or Nicardidil as an Adjunct to Percutaneous Coronary Intervention for ST-Segment Elevation Acute Myocardial Infarction

Masafumi Seguchi, Masafumi Myoishi, National Cardiovascular Ctr, Suita, Japan; Yosunori Shintani, Osaka Univ Graduate Sch of Medicine, Suita, Japan; Hiroshi Asanuma, Osamu Shintani, Osaka Univ Graduate Sch of Medicine, Suita, Japan; Tetsu Minamino, Osaka Univ Graduate Sch of Medicine, Suita, Japan; Jiseong Kim, National Cardiovascular Ctr, Suita, Japan; On behalf of the J-WIND investigators

Despite improved outcome with establishment of reperfusion therapy, heart failure and cardiovascular (CV) death remain significant risks after acute myocardial infarction (AMI). Limiting infarct size may reduce post-AMI risks. We evaluated the effects of nicorandil and ANP on infarct size and subsequent CV outcome. In 2 independent prospective, single-blind, placebo (PBO)-controlled, randomized studies conducted at 94 hospitals in Japan, subjects undergoing reperfusion therapy after AMI received either nicorandil (0.067mg/kg bolus injection, then 1.67 μg/kg/min 24-hr continuous infusion) or ANP (0.025 μg/kg/min continuous infusion) (PBO)-controlled, randomized studies conducted at 94 hospitals in Japan, subjects undergoing reperfusion therapy after AMI received either nicorandil (0.067mg/kg bolus injection, then 1.67 μg/kg/min 24-hr continuous infusion) or ANP (0.025 μg/kg/min continuous infusion) or matching placebo. Average follow-up was approximately 2.5 yrs. The primary endpoints were infarct size (create kinase mass (CKm) estimated by the area under the curve) and left ventricular ejection fraction (EF) evaluated by left ventriculography. Incidence of CV death, CV event or heart failure was the secondary endpoint. In all, 613 subjects received treatment with nicardidil (N=309) or PBO (N=304) and 603 subjects received ANP (N=290) or PBO (N=313);
Randomized Controlled Trial of Pulmonary Vein Antrum Isolation vs. AV Node Ablation with Bi-Ventricular Pacing for Treatment of Atrial Fibrillation in Patients with Congestive Heart Failure (PABA CHF)

Mohammed N Khan, Cleveland Clinic, Cleveland, OH; Pierre Jais, Hospital Cardiologique du Haut-Leveque, Bordeaux, France; Jennifer Cummings, Cleveland Clinic, Cleveland, OH; Prashanthan Sanders, Hospital Cardiologique du Haut-Leveque, Bordeaux, France; Josef Kautner, Institute for Clinical and Experimental Medicine, Prague, Czech Republic; Steven Hao, Sutter Pacific Heart Cntrs, San Francisco, CA; Sakis Themistoclakis, Umberto I Hosp, Mestre-Venice, Italy; Raffaele Fanelli, Domenico Potenza, Casa Sollievo della Sofferenza, San Giovanni, Rotondo, Italy; Dussana Wazni, Robert Schweikert, Wald Saliba, Cleveland Clinic, Cleveland, OH; Paul Wang, Amin Al-Samarrai, Mardock University Cardiocentur, Slovakia; Salah El Akl, Saint Louis University Heart Center, Saint Louis, MO; Gianfranco Galderisi, San Raffaele Hospital, Milan, Italy; Roberta Rognoni, Dana Darbari, Boston University School of Medicine, Boston, MA; Jonathan Chang, Swiss Heart Center, Bern, Switzerland; and the PABA Investigators

Background: Pulmonary vein isolation (PVI) is increasingly being used for treatment of atrial fibrillation. AV node ablation with bi-ventricular pacing (AVN-BIV) has been found to be superior to right ventricular pacing for treatment of atrial fibrillation. Methods: This prospective, multi-center clinical trial randomized patients with symptomatic, drug-resistant atrial fibrillation, EF ≤40% and NYHA III-II heart failure to either PVI or AVN-BIV. Patients were randomized to the PVI group at 3 months and to AVN-BIV at a second PVI. All patients underwent Minnesota Living with Heart Failure (MLWHF) questionnaire and 6-minute walk test. Follow-up period is 6 months with monitoring for both symptomatic and asymptomatic episodes of atrial fibrillation. Results: 35 patients underwent PVI and 36 patients underwent AVN-BIV with no one lost to follow-up at 6 months. Baseline characteristics did not differ between the groups. The trial reached its primary endpoints favoring the PVI group vs. the AVN-BIV group with improved MLWHF score at 6 months (61 vs. 79, p < 0.0001), longer 6-minute walk distances (345 vs. 301 m, p = 0.0002) and higher EF (35% vs. 29%, p = 0.0026). Freedom from atrial fibrillation in the PVI group was 89% and freedom from atrial fibrillation and antihypertrophic medications in the PVI group was 74% at 6 months. There were no major complications in either group. Conclusions: AVN-BIV results in marked improvement of quality of life, 6-minute walk test and echo parameters, all without pacemaker dependence from AV node ablation. This study supports the use of PVI for heart failure patients with drug-refractory AF.

N- Terminal pro- Type Natriuretic Peptide Improves the Management of Patients With Suspected Acute Decompensated Heart Failure: Primary Results of the Canadian Multicenter IMPROVE-CHF Study

Gordon W Moe, St Michael’s Hosp, Toronto, Canada; Hanna Zowall, Zowall Consulting, Montreal, Canada; Jonathan Howlett, Queen Elizabeth II Health Sciences Ctr, Halifax, Canada; Canadian IMPROVE-CHF study investigators

Background: Acute decompensated heart failure (ADHF) is an important clinical problem worldwide. The diagnostic utility of N-terminal pro-type natriuretic peptide (NT-proBNP) in ADHF has been documented but with the bulk of data derived from countries with relatively high heart health care resource utilizations. Hypothesis: We tested the hypothesis that the use of NT-proBNP improves the overall management of patients presenting with dyspnea to emergency departments (EDs) in a Canadian health setting, a model for universal health care. Methods: A multicenter, randomized, placebo-controlled, double-blind, multi-site trial in 31 EDs, enrolled 666 patients ≥18 years of age with dyspnea to ADHF between November 2008 and November 2009. On presentation to the ED, subjects were randomized to receive either NT-proBNP or placebo. Subjects had a median age of 67 years (IQR 56-75) and a median NT-proBNP level of 878 pg/mL (IQR 346-2520). Results: Median age was 75 years with 52% male. Median NT-proBNP level of the 227 subjects (47%) with final diagnoses of ADHF was 3097 pg/mL versus 461 pg/mL in those without, p < 0.0001. In establishing a correct diagnosis, adding NT-proBNP to clinical and diagnostic accuracy, the physician’s diagnostic accuracy characteristic curve increased from 0.86 to 0.95, p < 0.0001. At 60 days, 98 subjects (19.6%) either died or were hospitalized. Among those admitted to hospital from the ED, NT-proBNP at 72 hours predicted mortality (hazard ratio 1.06 per 1000 pg/mL change, 95% confidence intervals 1.01–1.10) and combined mortality and hospitalization (1.05, 1.02–1.08) at 60 days. Knowledge that NT-proBNP reduced the duration of ED visit (median 6.3 to 6.6 hours, p = 0.038), number of patients re-hospitalized (51 to 33, p = 0.044) and cost of all ED visits and hospitalizations ($US592 to $4361 per patient, p = 0.006).

Conclusions: In a universal health care system that mandates judicious resource allocation, the use of NT-proBNP improves the management of patients presenting to ED with suspected ADHF through the facilitation of diagnosis, reduction in cost and improvement in selected clinical outcomes.

Late-Breaking Clinical Trials III

The Alternans Before Cardiovore Defibrillator (ABCD) Trial: A Noninvasive Strategy for Primary Prevention of Sudden Cardiac Death Using T-Wave Alternans

Ottorino Costa, David S Rosenbaum, Mehrotra Cardiex Campi Case Western Reserve Univ, Cleveland, OH; Stephen H Hohnloser, J.W. Goethe Univ, Frankfurt, Germany; Malcolm Kirk, Brown Med Sch, Providence, RI; Bruce Lerman, Cornell Univ Med Ctr, New York City, NY; James Baker J, St Thomas Hosp, Nashville, TN; Barbars Selhurman, St Jude Inc, Sunnyvale, CA; Mary Dettmer, Mehrotra Cardiex Campi Case Western Reserve Univ, Cleveland, OH; for the ABCD Investigators

Guidelines for prevention of sudden cardiac death (SCD) based on left ventricular ejection fraction (LVEF) alone are limited by low therapeutic efficacy, as many ICDs never deliver therapy. Therapeutic efficacy is improved when an electrophysiologic study (EPS) is used with low LVEF for primary prevention of SCD. Since screening with invasive EPS is impractical, we tested the hypothesis that a noninvasive microvolt T wave alternans (MTWA) test can identify patients who benefit from ICDs with equal or greater accuracy than invasive EPS. The ABCD trial is a multicenter prospective study which enrolled 566 patients with ischemic cardiomyopathy (LVEF ≤0.40, non-sustained VT, and no prior ventricular arrhythmias. All patients underwent a MTWA test and an EPS. An independent Core Laboratory interpreted all tests. ICDs were implanted if either test was positive. An independent Events Committee adjudicated all events. Mean age was 65 ± 10 years, LVEF 0.28 ± 0.07, and 84% were male. Patients were in either NYHA class 1 (30%), 2 (50%), or 3 (20%) CHF. Beta-blockers were used in 86%, and ACE inhibitors or ARBs in 88% of patients. Median follow up was 1.9 years. Sixty-five patients (11%) met the primary endpoint of appropriate ICD therapy (n = 1101). The sensitivity, specificity, PPV, NPV, and positive predictive value of 1 year were 85%, 61%, 79%, and 9%, respectively. The negative predictive value at 1 year was 95% for both. In addition, event rates were higher in patients with ICD therapy guided by MTWA+ compared to MTWA- tests (HR 1.6, p = 0.03) as well as in patients with a EPS+ vs. a EPS− (2.5, p = 0.07). The event rate for patients with both negative MTWA test and EPS was very low (2%). In conclusion, ANP as an adjunct therapy to PCI reduced infarct size and improved outcome in patients with a first AMI; nocardial may provide further cardioprotection.

First Randomized Placebo-Controlled Myoblast Autologous Grafting in Ischemic Cardiomyopathy (MAGIC Trial)

Philippe Menasché, Assistance Publique-Hôpitaux de Paris, Hôpital Éminence Georges Pompidou, Dept of Cardiovascular Surgery, Paris, France; On behalf of the MAGIC Multi-Ctr Investigator Group

Several early-phase clinical studies have demonstrated the feasibility of transplanting autologous skeletal myoblasts in postinfarction scars and revealed a potential risk of arrhythmias. However, because of their design, these studies fail to conclusively establish a causal relationship between arrhythmias and myoblast injections, nor provide clear evidence for functional efficacy. To address these issues, we have undertaken the Myoblast Autologous Grafting in Ischemic Cardiomyopathy (MAGIC) trial to investigate the safety and efficacy of 2 doses of skeletal myoblasts, as compared to placebo control, in the treatment of ischemic heart failure. This study was a multicenter, randomized, placebo-controlled, double-blind, multicentre trial. 581 patients were included when meeting the following 3 major criteria : 1) LV dysfunction defined by an EF ≤0.35, myocardial infarction with more than 2 contiguous akinetic scarred segments unresponsive to dobutamine stress and an indication for concomitant coronary artery bypass surgery. Baseline characteristics: Baseline EF = 24%. 

0.05% test (t = 0.012). The free rate of CV event analysis showed that the free rate of re-hospitalization due to heart failure in ANP was statistically different from placebo with a lower rate of 0.378). In conclusion, ANP as an adjunct therapy to PCI reduced infarct size and improved outcome in patients with a first AMI; nocardial may provide further cardioprotection.
Background: Treatment of coronary in-stent restenosis (ISR) by balloon dilatation, brachytherapy, or drug-eluting stents is hampered by a high incidence of recurrent ISR. We assessed the efficacy and safety of a paclitaxel-coated balloon in coronary ISR. **Methods:** We enrolled 108 patients in two separately randomized, double-blind multicenter trials on efficacy and safety of a paclitaxel-coated balloon (3 μg/mm² balloon surface; Paccocath), applying an identical protocol. Patients were treated by the drug-coated or an uncoated balloon with a balloon inflation time of 60 sec. The main inclusion criteria were diameter stenosis of >50% and <35 mm length with a vessel diameter of 2.5 to 3.5 mm. The primary endpoint was angiographic late lumen loss. Secondary endpoints included binary restenosis rate and major adverse cardiac events (MACE). **Results:** Multivessel disease was present in 80% of patients in both groups. Quantitative coronary angiography revealed no differences in baseline parameters. After six months, the late lumen loss was 0.8 ± 0.8 mm in the uncoated balloon group versus 0.1 ± 0.5 mm (p < 0.01) in the drug-coated balloon group. Binary restenosis rate (p = 0.01), and MACE after 6 and 12 months (p < 0.01) were correspondently less frequent in the drug-coated balloon group. Most MACE were related to the need for target lesion revascularization at 6 months. **Conclusion:** Treatment of coronary ISR with paclitaxel-coated balloon catheters leads to a significant reduction of repeated restenosis. These data suggest that restenosis inhibition by local drug delivery does not require stent implantation and sustained drug release at the site of injury.

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SLX-4090: First Human Experience and Proof of Concept for an Enterocyte-Specific Microsomal Triglyceride Transfer Protein Inhibitor

**Introduction:** Microsomal triglyceride transfer protein (MTP) facilitates the formation and transfer of chylomicrons out of the intestine and the liver. Previous MTP inhibitors caused transfer of chylomicrons out of the intestine and the liver. Previous MTP inhibitors caused no systemic absorption thus avoiding mechanism based toxicity in the liver. We report the results from the first study in humans including safety, tolerability and effects on multivessel disease. **Background:** Microsomal triglyceride transfer protein (MTP) inhibition is a very accurate picture of the placebo effect in subjects with IC and PAD. The uniformity of the results between the two groups suggests that these findings are a very accurate picture of the placebo effect in subjects with IC and PAD.

**Results:** A total of 157 patients were randomized and treated. Their mean age was 65.3 ± 7.7 years, 76% were male, 85% were Caucasian, 38% were diabetic, 31% were current and 55% were former smokers. For the primary endpoint, the PWT in the VLTS-934 group at baseline and Day 90 was 5.1 (±3.2) min and 6.2 (±3.7) min respectively, and in the control group was 5.0 (±2.2) min at baseline and 6.1 (±3.3) min at Day 90; p = 0.06 between groups. The baseline and Day 90 mean ABIs in the VLTS-934 group were 0.65 ± 0.18 and 0.71 ± 0.24 respectively, and 0.71 ± 0.24 and 0.7 ± 0.2 respectively in the control group; p = 0.87. Similarly, the other secondary efficacy endpoints were not statistically significantly different between groups. Serious adverse events were similar in both groups. **Conclusion:** VLTS-934 did not significantly improve IC in subjects with PAD compared to saline control. The results of the analysis of the results between the two groups suggest that these findings are a very accurate picture of the placebo effect in subjects with IC and PAD.