1026-104 **The Effect of Vardenafil, a Selective PDE5 Inhibitor, on Ischemic Threshold, Exercise Tolerance, and Circulatory Responses During Treadmill Exercise in Men With Stable Angina Pectoris**

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Background: Erectile dysfunction (ED) is common among men with CAD. Vardenafil (5, 10, and 20mg) is an efficacious oral treatment for ED. The effects of vardenafil 10mg on exercise parameters in patients with stable angina and reproducible exertional cardiac ischemia were previously evaluated; this study examined the effects of vardenafil 20mg in a similar patient population.
Methods: In this double-blind, crossover, single-dose, multicenter study, 39 men randomized to vardenafil 20mg or placebo were evaluated by symptom-limited exercise treadmill test (ETT) one hour post-dose, the time of maximal drug exposure. Nitrates were prohibited during the study.
Results: Majority of men (mean age 63.8 y [range 48-80 y]) received beta-blockers (29/39), aspirin (35/39) and lipid lowering drugs (29/39). Data derived during exercise is shown.

	Vardenafil 20 mg		Placebo	
Parameter	n	Value	n	Value
Treadmill Exercise Time*, sec	36	414±114	36	411±124
Time to Angina Pectoris*, first awareness, sec	36	354±137	36	347±143
Time to ST-Segment depression≥ 1 mm Δ from BL*, sec	33	364±101	36	366±105
Rate-pressure product, peak exercise*, mmHg x BPM x 10^3*	39#	19.2±5.2	38 #	19.3±4.3

*-mean ±SD, p>0.05, based on LS geometric mean ratio of vardenafil/placebo. #-includes 3/2 patients in vardenafil/placebo groups respectively,excluded from ETT analysis because of protocol violations.

Vardenafil was well tolerated. The most common adverse events during vardenafil treatment (facial flushing and headache) were mild or moderate and transient. One patient receiving vardenafil exhibited post-exercise transient hypotension and dizziness which resolved following oral fluid replacement.
Conclusion: Vardenafil 20mg did not impair stable CAD patients' ability to exercise or alter ischemic threshold at effort levels considered equal to or greater than sexual intercourse.

1026-105 **An Examination of Atorvastatin Safety When Used in Combination With Verapamil: Evidence From 44 Completed Clinical Trials**

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Background: Verapamil is a widely prescribed calcium channel blocker used for the treatment of angina, hypertension and supraventricular arrhythmias. Recently, safety questions have been raised about the concomitant utilization of verapamil with statins.
Methods: Atorvastatin is a well established statin that effectively lowers LDL cholesterol and triglycerides across the 10-80 mg dose range. We investigated whether there was any indication of an interaction between atorvastatin and verapamil as indicated by an increased rate of common statin-associated adverse events in the atorvastatin clinical trial program.
Results: To date, the program consists of 44 completed clinical trials with 9416 patients that have received atorvastatin. Of these 9416 patients, 292 (3.1%) have received concomitant verapamil (76% on 10 mg atorvastatin and 20% on 80 mg atorvastatin). There were no incidences of myopathy, rhabdomyolysis or CPK elevations >10×ULN among the 292 atorvastatin/verapamil patients. The rate of treatment-emergent myalgia in patients taking atorvastatin/verapamil was 8/292 (2.7%). Of the patients taking atorvastatin/verapamil, 3/292 (1.0%) were thought to have myalgia that was treatment-related. This rate of myalgia is comparable to the overall rate of treatment-related myalgia seen in the entire 9416 patients exposed to atorvastatin in the clinical program (1.9%). Persistent ALT elevations >3×ULN occurred in 1/292 (0.3%) of the atorvastatin/verapamil patients, an incidence comparable to the overall rate of 0.5% seen in the entire 9416 atorvastatin cohort across all doses.
Conclusion: In conclusion, data from the atorvastatin clinical trial program does not currently indicate an increased rate of muscle or hepatic adverse events when atorvastatin is used concomitantly with verapamil. Additional data will be collected with over 44000 patients currently ongoing in clinical trials with atorvastatin.

POSTER SESSION

1027 Cardiac Arrest and Resuscitation

Sunday, March 30, 2003, Noon-2:00 p.m.
McCormick Place, Hall A
Presentation Hour: Noon-1:00 p.m.

1027-89 **Safety and Efficacy of Nesiritide in the Treatment of Decompensated Heart Failure in Observation Patients**

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Background: Nesiritide (NES), B type natriuretic peptide, has been demonstrated to have hemodynamic and other clinical benefits for patients (pts) with decompensated heart failure. There has been little investigation of this agent for pts being treated in observation or similarly staffed units. The purpose of this study was to evaluate the safety, efficacy, and economic benefits of NES therapy in the less monitored setting of the Emergency Department (ED).
Methods: Multicenter, randomized, double blinded, pilot study of pts with decompensated heart failure evidenced by dyspnea at rest or on walking less than 20 feet. Pts were identified and randomized within 3 hours of ED arrival. Initial treatment was begun with diuretics, O_2, and, if desired, morphine or non-parenteral nitrates. ACE Inhibitors were withheld for 3 hours. Other vasodilators and inotropes, discouraged for the first 12 hrs, could be used after 3 hrs. Pts received NES or placebo for at least 12 hours. Pts were either admitted or discharged after a maximum of 24 hours in the ED but could be continued on study drug in the hospital.
Results: 250 pts were randomized; 237 received study drug. 56% male, mean age 65.6 years; 47% Caucasian and 46% African-American. 61% NYHA Class III/IV at baseline and average EF 35%. 33 % had preserved systolic function. Mean baseline BNP level was 747 pg/ml. Admission rate for NES was 49% vs. 55% for placebo. Admission rate for CHF was lower for NES (30%) than placebo (38%). Of hospitalized pts, 10% NES and 23% placebo were rehospitalized within 30 days (p=.058). The total LOS over 30 days, including the initial visit for pts hospitalized and then rehospitalized, was 5.5 days for NES vs. 10.2 days for placebo (p=.052). There was no significant difference in drug termination, symptomatic hypotension, ventricular arrhythmias, or death between the two groups. The overall cost of care was lower in the NES group, driven by decreased LOS and lower readmission rates over the 30 day study period, which neutralized the cost of drug.
Conclusions: NES is safe and effective in the treatment of emergency department/observation pts. The cost of adding NES is balanced by decreased costs associated with admission and readmission.

1027-90 **The Resuscitative Value of B-Type Natriuretic Peptide in Patients With Out-of-Hospital Cardiac Arrest Due to Cardiac Causes**

Ken Nagao, Nariyuki Hayashi, Takeo Mukouyama, Ikuyoshi Watanabe, Sumito Oguchi, Satoru Kikuchi, Shigemasa Tani, Kazuhiro Watanabe, Kiyoshi Iida, Takeo Anazawa, Takashi Miyamoto, Tadamasa Nosaka, Katsuo Kanmatsuse, Nihon University School of Medicine, Tokyo, Japan

Background: B-type natriuretic peptide (BNP) is released by the ventricular myocardium in response to increased wall tension. Although the circulating level of this neurohormone has been shown to have a prognostic value in either congestive heart failure or acute coronary syndromes, no data are available for a resuscitative value in out-of-hospital cardiac arrest.
Methods: We conducted a prospective study of 401 patients whose BNP was measured on arrival at the emergency room after out-of-hospital cardiac arrest due to cardiac causes. The primary end point was survival to hospital discharge.
Results: A total of 52 of the 401 patients survived to discharge from the hospital and the BNP level was lower among such patients than among those who died (mean+/-SD, 74+/-128 vs. 260+/-292pg/ml, p<0.001). The BNP levels ranged from 2 to 2620pg/ml, with a mean+/-SD of 236+/-283pg/ml, a median of 152pg/ml, and 25th and 75th percentile values of 34 and 392pg/ml, respectively. The unadjusted rate of the survival decreased in a stepwise fashion among patients in increasing quartiles of BNP levels with quartile 1 at 34% vs. quartile 2 at 10% vs. quartile 3 at 7% vs. quartile 4 at 1% (p<0.001). This association remained significant in subgroups of patients with witnessed arrest, bystander cardiopulmonary resuscitation and ventricular fibrillation in initial cardiac rhythm (p<0.001, respectively). After adjustment for independent predictors of resuscitation, the odds ratios for the survival in the second, third and fourth quartiles of BNP were 0.14 (95% CI, 0.04 to 0.45), 0.10 (95% CI, 0.03 to 0.36), and 0.008 (95% CI, 0.0 to 0.17). A value of 100pg/ml or less for BNP was the significant independent predictor of the survival with an adjusted odds ratio of 10.9.
Conclusions: The measurement of BNP on arrival at the emergency room provides predictive information for survival to hospital discharge in patients with out-of-hospital cardiac arrest due to cardiac causes.