Effect of Atorvastatin, Sildenafil and Their Combination on Endothelial Function

	Baseline	S	A	CT
Brachial artery (mm)	4.37±0.4	4.38±0.3;	4.37±0.2	4.38±0.4
FMD (%)	6.8±0.9	10.97±0.7*	11.2±0.6*	12.5±0.9**
Nitrite+nitrate (Nox)	41.3±10.6	49.3±6.7*	48.7±7.3*	52.3±9.7**
Endothelin-1(pg/ml)	3.3±0.5	2.8±0.7*	2.4±0.6**	2.4±0.8**
*=p<0.05	**=p<0.01			

1141-197 **Detection of Aspirin Resistance in Subjects With Multiple Risk Factors for Cardiovascular Disease**

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Background: Aspirin is known to reduce the risk of cardiovascular events by 25% in patients with arterial vascular disease. However, the phenomena of "aspirin resistance" may result in a higher rate of adverse outcomes in such patients. We sought to determine the prevalence of aspirin resistance with the novel cartridge for the Ultegra Rapid Platelet Function Analyzer (RPFA-ASA) after one dose of non-enteric coated aspirin (325-mg) in subjects with multiple risk factors for cardiovascular disease.
Methods: Data from 148 subjects were analyzed. Platelets were assessed twice at baseline (pre-aspirin), and after 2-30 hours (post-aspirin). Aspirin response units (ARU) stimulated by cationic propyl gallate were measure by Ultegra RPFA-ASA, while 5μM epinephrine-induced conventional aggregometry was used as a reference.
Results: A single dose of aspirin decreases ARU from 647±95 to 436±69, matching closely the diminished aggregation from 72±21% to 25±10%. Figure 1 demonstrates the ranges of responses in ARU's for patients prior and after aspirin ingestion. There is an area of overlap where both pre-ASA and post-ASA measurements fall, and it is not possible to assay with any assurance that platelet function has been effectively suppressed by the ASA, regardless of the test result prior to therapy. The use of the equivocal (yellow) zone increases the reliability of a posteriori assignment of a patient into an effectiveness group, since it refuses to supply a decision in cases where there is high variability in the decision. The range of 550 and above as a non-responder, 500 to 550 as the equivocal zone, and less than than 550 as an aspirin responder results in the optimal boundaries to minimize the errors-of-classification.
Conclusion: The timely detection of aspirin resistance is critical for adequate management of antithrombotic regimens. The Ultegra RPFA-ASA is a novel, fast method that could be used in clinical practice for monitoring of aspirin efficacy, and early detection of aspirin resistance.

1141-198 **Etoricoxib Has No Adverse Effects on Biomarkers of Cardiovascular Risk in Patients With Osteoarthritis**

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BACKGROUND:Selective cyclooxygenase-2 (COX-2) inhibitors are effective anti-inflammatory agents, and their use results in a lower rate of ulcers and their complications compared to non-selective NSAIDs. However, questions have been raised about a possible adverse effect on CV outcomes.
METHODS: 433 patients with osteoarthritis were randomized (double-blind) to etoricoxib 90 mg qd, celecoxib 200 mg bid, ibuprofen 800 mg tid, or placebo for 12 weeks. LDL cholesterol, homocysteine, fibrinogen, and CRP were measured at baseline, and at 6 and 12 weeks. The primary hypothesis was that etoricoxib is non-inferior to placebo in its effect on all four biomarkers based on an "on-treatment" analysis. Non-inferiority margins (20% for LDL, fibrinogen and homocysteine, and 80% for CRP) were pre-defined for each biomarker based on published data. RESULTS: Etoricoxib was non-inferior to placebo on all four biomarkers after 12 weeks (Table). Etoricoxib was also non-inferior to celecoxib and ibuprofen. The effect of etoricoxib on CRP was greater in patients who smoked (46% reduction vs placebo), with diabetes (51%) or with higher Framingham CV risk score (32%).
CONCLUSION: Etoricoxib was comparable to placebo, celecoxib, and ibuprofen in its effect on four established biomarkers of CV risk. While clinical outcomes data will provide a more definitive CV safety profile for COX-2 inhibitors, these data provide reassurance that selective COX-2 inhibition does not have an adverse effect on these known markers of CV risk.

Biomarkers	Mean Change on Log-scale (SE)			Relative difference in geometric mean * (97.5% CI)
	Etoricoxib (E)	Placebo (P)	Difference (E-P) (97.5% CI)	
CRP (mg/mL)	-0.09 (0.09)	-0.01 (0.09)	-0.08 (-0.36, 0.20)	-7.8 (-30.5, 22.4)
LDL (mg/dL)	-0.02 (0.02)	0.02 (0.02)	-0.04 (-0.11, 0.03)	-4.0 (-10.6, 3.2)
Homocysteine (μ mol/L)	-0.03 (0.03)	0.01 (0.03)	-0.04 (-0.12, 0.05)	-3.9 (-11.6, 4.6)
Fibrinogen (mg/dL)	-0.05 (0.02)	-0.01 (0.02)	-0.04 (-0.10, 0.02)	-3.7 (-9.4, 2.3)
*relative difference=exp(mean difference on log-scale)-1				

POSTER SESSION

1142

Cardiac Remodeling in Hypertension

Tuesday, March 09, 2004, Noon-2:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 1:00 p.m.-2:00 p.m.

1142-177 **Antecedent Hypertension and the Risk of Subsequent Left Ventricular Remodeling After Acute Myocardial Infarction: Insights From the Survival and Ventricular Enlargement Trial**

Satish Kenchaiah, Marc A. Pfeffer, Martin St. John Sutton, Ted Plappert, Jean-Lucien Rouleau, Gervasio A. Lamas, Zion Sasson, John O. Parker, Edward M. Geltman, Eugene Braunwald, Scott D. Solomon, Brigham and Women's Hospital, Boston, MA

Background: While hypertension increases the risk of myocardial infarction (MI), whether antecedent hypertension influences the risk of subsequent left ventricular (LV) enlargement in survivors of an acute MI with LV systolic dysfunction is unclear.
Methods: We assessed echocardiographic evidence of ventricular remodeling between baseline (mean±SD, 11±3 days) and 2 years after acute MI in 122 hypertensive (defined as history of treated hypertension, or baseline systolic BP ≥140, or diastolic BP ≥90 mm Hg) and 334 nonhypertensive participants of the Survival and Ventricular Enlargement (SAVE) echo substudy.
Results: As compared with nonhypertensives, the baseline heart size, defined as the sum of the average short and long axis LV cavity areas (LVCA), was similar (70.1±11.9 vs. 68.8±11.2 cm^2, p=0.33 at end diastole; 50.1±11.3 vs. 48.8±10.8 cm^2, p=0.31 at end systole), but short axis LV myocardial area (LVMA, 24.7±4.3 vs. 25.7±5.0 cm^2, p=0.043) and wall thickness (LVWT, 1.15 ±0.16 vs. 1.21±0.17 cm, p=0.004) were higher among hypertensives. The infarct segment lengths were similar in the two groups (p=0.22). Whereas end-diastolic and end-systolic LVCA increased significantly in both groups from baseline to 2 years (p ≤0.001), the increase was significantly greater in hypertensives as compared with nonhypertensives (+5.6±11.5 vs. +2.2±10.7 cm^2, p=0.005 at end diastole; +6.23±12.75 vs. +2.94±11.4 cm^2, p=0.012 at end systole). There was no concomitant difference in change in LVMA or LVWT between the two groups (p>0.30). After adjusting for study medication (captopril), age, body mass index, peak creatine kinase, diabetes, smoking, prior MI, infarct size and location; antecedent hypertension was associated with a doubling of the risk of LV dilatation, defined as an increase of >1.96 times SDs of measurement reproducibility of end-diastolic or end-systolic LVCA (50.8% vs. 37.7%, OR 2.02, 95% CI 1.23-3.31, p=0.006). There was no effect modification of this association by diabetes, infarct size, or captopril use (all p-values for interaction >0.10).
Conclusions: Antecedent hypertension is associated with an increased risk of LV enlargement in survivors of an acute MI with LV systolic dysfunction.

1142-178 **The G1675A Gene Polymorphism of the Angiotensin II Type 2-Receptor Gene Influences Cardiac Structural Response to Antihypertensive Therapy**

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Introduction: In vitro, the angiotensin II type 2 receptor (AT2-R) exerts antiproliferative effects in the cardiovascular system. Moreover, the G1675A gene polymorphism of the AT2-R has been shown to influence left ventricular structure in essential hypertensive subjects. We hypothesized that this gene polymorphism may also alter the cardiac structural response to antihypertensive therapy, in particular to agents interfering with the renin-angiotensin-system.
Methods: In the Cardiovascular Irbesartan Project (CVIP), a double blind randomized clinical study, patients with mild-to-moderate essential hypertension and early target organ damage as evidenced by an increased intima media thickness (IMT) of the common carotid artery (0.8-1.5 mm) were treated with either irbesartan or atenolol for 18 months. The G1675A genotype of the AT2-R gene was determined by a 5' nuclease allelic discrimination assay using real-time PCR in 112 subjects.
Results: At baseline, blood pressure and left ventricular mass index (LVMI) were similar between genotypes. In addition, after 6 and after 18 months, blood pressure control was similar between genotypes. However, G allele carriers (males with G genotype and females with GG or GA genotype, n=62) showed an increase in LVMI while hemizygous males and females with the AA genotype (n=50) showed a decrease in LVMI (+2.5±20.4 vs -8.8±25.0 g/m^2, p=0.02 after 6 months and +6.6±26.3 vs -11.4±21.9 g/m^2, p=0.002 after 18 months). These differences were also observed in both treatment subgroups to a similar extent.
Conclusion: The A allele of the G1675A polymorphism of the AT2-R was associated with a favorable response of cardiac structure to antihypertensive therapy, regardless of the type of treatment.