11:30 a.m.

879-5 **Beta Radiation With Direct Stenting: Final Results of the BRIDGE Trial**

Patrick W. Serruys, William Wijns, Ivan de Scheerder, Paul A. van den Heuvel, Wolfgang Rutsch, Helmut D. Glogar, Carlos Macaya, Pierre H. Materne, Heike Vonhausen, Patricia C. Otto-Terlouw, Erasmus Medical Center, Rotterdam, The Netherlands

The BRIDGE study is a multicenter, randomized controlled clinical trial evaluating the acute and long-term efficacy of intravascular brachytherapy (VBT) with P-32 immediately following direct stenting (20 Gy 1 mm inside the coronary wall).
VBT at the time of stent implantation for de novo lesions has not yielded good results and is presently abandoned. We wanted to revisit this approach and have tried to optimize all procedural steps: ideal case selection, use of IIb-IIIa blockers, direct stenting, avoidance of edge damage, source centering, IVUS guided dosimetry and adequate radiation coverage. Patients were randomized to VBT or no-VBT. The sample size has at least 84% power to detect a 50% decrease in loss of MLD as assessed by QCA at 6 months (primary endpoint). The secondary endpoints are clinical and safety outcomes (1, 6 and 12 mths), restenosis (50% diameter stenosis), remodelling and neo-intimal hyperplasia by IVUS, late thrombotic occlusion (up to 12 mths). Inclusion criteria: stable or unstable angina or documented silent ischemia with one or two successfully stented de novo lesions at least 2.5-4.0 mm in diameter and up to 15mm long. Between Feb 2001 and Mar 2002, 112 patients (1.04 lesions/pt) were randomized to VBT or no-VBT at 8 sites in Europe. Of the VBT patients 93% were successfully treated. Baseline characteristics: age 60.5 yrs, male 79.8%, unstable 25.5%, stable angina 68.2%, silent ischemia 5.5%. Pre-procedure (N=81): mean vessel size was 2.84 vs. 2.85 mm, MLD was 0.95 vs. 1.05 mm and lesion length was 10.9 vs. 11.0 mm (VBT vs. no-VBT). Post-procedure: mean vessel size was 2.83 vs. 2.82 mm and MLD was 1.78 vs. 2.04 mm. Stented segment: mean vessel size was 3.04 vs. 3.03 mm, MLD post was 2.69 vs. 2.67 mm, diameter stenosis was 11 vs. 12 % (VBT vs. no-VBT). Irradiated segment (defined by the length of the effective radiation source, full dose prescribed): mean vessel size was 2.98 mm, MLD post was 2.05 mm, diameter stenosis was 32%. MACCE up to 30 days: death 0%, Q-MI 1.8%, non-Q-MI 2.7%, CABG 0%, re-PTCA 0.9% and 1.8% sub-acute occlusion.
The final results, including 12 months follow-up, will be presented during the meeting.

11:45 a.m.

879-6 **Sirolimus-Eluting Stent or Intracoronary Brachytherapy to Treat In-Stent Restenosis**

Fausto Feres, Juan S. Munoz, Alexandre A. Abizaid, Rodolfo Staico, Luiz A. Mattos, Galo Maldonado, Marinella Centemero, Luiz F. Tanajura, Aurea J. Chaves, Ibraim Pinto, Andrea S. Abizaid, Amanda Sousa, Jose Eduardo M. Sousa, Institute Dante Pazzanese of Cardiology, Sao Paulo, Brazil

Background: Intracoronary Beta-Radiation Therapy (BT) has been shown to be effective to treat in-stent restenosis (ISR) in large randomized clinical trials. Drug- eluting stents (DES) also have been successfully used to treat ISR in small pilot studies. The purpose of this study is to report clinical and angiographic outcomes of patients (Pts) with ISR treated either with balloon angioplasty followed by BT or DES.
Methods: From March 2001 to April 2002, 50 consecutive pts with ISR were treated either with Sirolimus- eluting stent or BT (Novoste,Beta-Cath).The first 25 pts were treated with DES (one or two 18 mm Cypher stent were used per patient) and the second 25 treated with BT (40 mm source). Angiographic quantifications were performed in all pts at baseline (Post) and the follow-up (FUP) (12 months for DES and 6 months for BT).
Results: Clinical FUP was available at 12 months for all pts in DES group and for 22 (88%) in the BT group who completed 6 months FUP. 100% of DES group and 82% of the BT group were free of MACE (TVR, AMI or death)-p=0.04. Angiographic FUP was done in all DES group at 12 months and 86% of the pts in BT group (19/22).

Angiographic Results(mm)	DES(n=25)	BT(n=19)
In-lesion length	13.66±7.80	16.74±3.63
Reference Diameter Post	2.8±0.36	2.70±0.35
MLD Pre	1.05±0.31	1.08±0.34
MLD in-segment Post	2.35±0.37	1.98±0.30*
MLD in-stent Post	2.72±0.31	1.99±0.31*
%DS Pre	62.06±10.71	63.51±8.90
%DS in-segment Post	16.13±8.14	28.54±7.94*
%DS in-stent Post	2.56±9.21	29.73±8.28*
Acute gain	1.67±0.34	0.91±0.43*
Reference Diameter FUP	2.78±0.34	2.62±0.33
MLD in-segment FUP	2.19±0.56	1.49±0.24*
MLD in-stent FUP	2.36±0.57	1.90±0.31*
Late loss in-segment	0.16±0.42	0.49±0.13*
Late los in-stent	0.35±0.45	0.10±0.29*
Angiographic restenosis	1(4%)	3 (15.7%)

* $p \leq 0.05$ vs. DES. MLD: minimal lumen diameter. %DS: % Stenosis diameter.
Conclusions: DES group presented better acute and late results (larger MLD post, FUP and acute gain). Although BT group had a smaller late loss in-stent, angiographic restenosis and MACE were smaller in the DES group, because of late loss in-segment in this group was much smaller.

ORAL CONTRIBUTIONS

880FO Featured Oral Session...New Insights in Pharmacology for Percutaneous Coronary Intervention

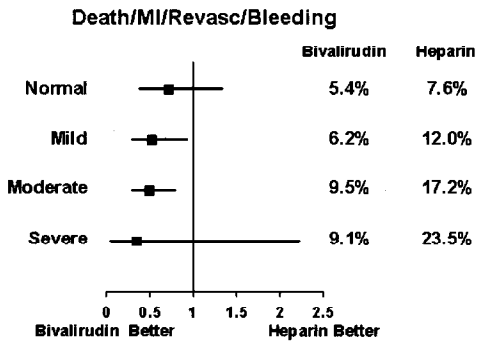
Wednesday, April 02, 2003, 10:30 a.m.-Noon
McCormick Place, Grand Ballroom S100 BC

10:45 a.m.

880FO-2 **Bivalirudin Provides Increasing Benefit With Declining Renal Function in Percutaneous Coronary Intervention: A Meta-Analysis of 5,035 Patients Enrolled in Three Randomized Trials**

Derek P. Chew, Deepak L. Bhatt, Peter B. Berger, Tim Henry, Peter A. McCullough, Frederick Feit, John A. Bittl, A. Michael Lincoff, Flinders Medical Center, Adelaide, Australia, The Cleveland Clinic Foundation, Cleveland, OH

Background: Chronic kidney disease is associated with an increased risk of both ischemic and bleeding events during PCI. Bivalirudin reduces both bleeding and ischemic complications. We sought to assess the magnitude of benefit in patients stratified by renal function.
Methods: We performed a meta-analysis of three randomized trials (BAT, REPLACE-1 and CACHET) comparing bivalirudin with heparin during PCI in which 5035 pts were enrolled. Stratification by renal function was performed by estimated glomerular filtration rate (eGFR) as determined by the Cockcroft-Gault equation: >90mls/min [n=1578; 31%]; 90-60mls/min [n=2163; 43%], 59-30 mls/min [n=1255; 25%], <30ml/min [n=39; 1%]. Trial specific eGFR strata for death, MI revascularization and hemorrhage were combined with a random-effects model.
Results: Ischemic and bleeding event rates increased with declining eGFR. Across strata, the relative benefit of bivalirudin vs. heparin with respect to ischemic events [>90: 0.79, 90-60:0.73, 59-30: 0.77, <30: 0.81], and bleeding events [>90: 0.45, 90-60:0.40, 59-30: 0.46] was maintained. Consequently, the benefit in terms of absolute ischemic and bleeding events increased with declining renal function (interaction p=0.044).
Conclusion: Renal dysfunction remains a prevalent risk factor for ischemic and bleeding events among patients undergoing PCI. Bivalirudin provides greater absolute benefit in reducing these adverse events in patients with impaired renal function.



11:00 a.m.

880FO-3 **A Prospective, Randomized Placebo-Controlled Multicenter Trial Evaluating Fenoldopam Mesylate for the Prevention of Contrast Induced Nephropathy: The CONTRAST Trial**

Gregg W. Stone, Peter McCullough, James Tumlin, Hooman Madyoon, Patrick Murray, Andrew Wang, A. Alan Chu, Gary Schaer, Melissa Stevens, Robert L. Wilensky, William W. O'Neill, Norman Lepor, Cardiovascular Research Foundation and Lenox Hill Heart and Vascular Institute, New York, NY

Background. Contrast-induced nephropathy (CIN) is common in pts with baseline chronic renal insufficiency undergoing invasive cardiac procedures, and is a powerful predictor of early and late morbidity and mortality. Fenoldopam mesylate is a selective dopamine-1 agonist that preserves renal medullary blood flow, and has shown promise in small studies in preventing CIN.
We therefore performed a large, multicenter, prospective randomized trial to evaluate this agent in pts at risk for CIN.
Methods. 315 pts at 28 U.S. centers with a baseline creatinine clearance (CrCl) of <60 cc/min not on dialysis undergoing cardiac catheterization ± angioplasty were hydrated and randomized 1:1 to I.V.fenoldopam (0.05 ug/kg/min titrated up to 0.10 ug/kg/min) vs. matching placebo, starting 1 hour prior to angiography and continuing for 12 hours thereafter. Serum creatinine levels were measured at baseline, and at 1, 24, 48 and between 72-96 hours following completion of study drug, and analyzed at a central biochemistry lab. The primary endpoint was the incidence of CIN, defined as an increase in serum cre-

atinine of ≥25% from baseline during this 96 hour period. The trial was powered to detect a reduction in the primary endpoint from 30% to 15%. Secondary endpoints included hospital length of stay, adverse cardiac events, re-hospitalization and need for dialysis within 30 days.

Results. In the pooled population, mean age was 70 ± 11 years, 34% were female, 51% had diabetes, 87% hypertension, 50% prior MI, and 48% prior CHF. The baseline CrCl was 29.2 ± 10.1 cc/min (range 7.5-57.5). Mean contrast dose was 164 ± 155 cc. The mean hospital length of stay was 4.0 ± 5.9 days. Within 30 days, 2.3% required dialysis, 19.2% were re-hospitalized, and 3.2% of pts died. CIN within 24-96 hours of drug, the primary endpoint, occurred in 30.5% of pts.

Conclusions. Despite hydration and contemporary catheterization techniques, CIN is common after invasive cardiac procedures in a population with baseline renal insufficiency and portends a poor prognosis. The results of CONTRAST, which examined the utility of fenoldopam mesylate, a specific D1 agonist, for the prevention of CIN will be unblinded for the first time for presentation in March 2003.

11:15 a.m.

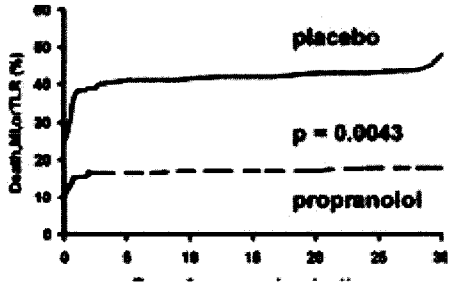
880FO-4 **Intracoronary Beta-Blocker Protects the Distal Myocardium During Percutaneous Coronary Intervention**

Fen Wei Wang, Abdulfatah Osman, Javier Otero, George A. Stouffer, Sergio Waxman, Adnan Afzal, Angelo Anzuini, Barry F. Uretsky, The University of Texas Medical Branch, Galveston, TX

Background: Experimental studies have shown that IV beta blockers given before coronary artery occlusion significantly reduce myocardial injury. We tested the hypothesis that intracoronary (IC) propranolol (0.015 mg/kg) pre-coronary intervention (PCI) reduces myocardial necrosis (MI) and short-term adverse outcomes after PCI. **Methods** Patients (n=150) undergoing elective or urgent PCI were randomly assigned in a prospective double-blind fashion to receive either IC propranolol (n=75) or placebo (n=75). **Results** Major adverse events through the first 30 days are shown in the table and figure. **Conclusion**: Intracoronary administration of propranolol significantly reduces the incidence of MI after PCI, improves short-term clinical outcomes, and suggests its routine use during PCI.

30 day Results (% of patients)

	Propranolol (n=75)	Placebo (n=75)	P value
Elevated CK-MB	17	36	0.01
Elevated Troponin T	13	33	0.005
Death	0	0	NS
Recurrent MI	1	3	NS
Urgent TLR	0	3	NS



11:30 a.m.

880FO-5 **Marked Survival Benefit Associated With Statin Pretreatment Prior to Percutaneous Coronary Intervention Is Dependent Upon the Preprocedural Inflammatory Status**

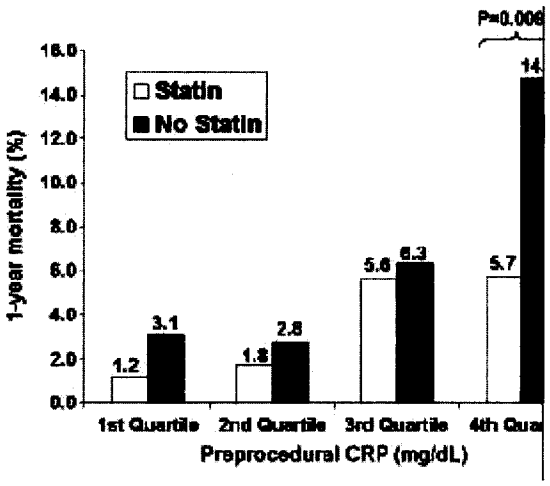
Albert W. Chan, Deepak L. Bhatt, Derek P. Chew, Joel Reginelli, Deepak P. Vivekananthan, Jakob P. Schneider, Eric J. Topol, Stephen G. Ellis, The Ochsner Clinic Foundation, New Orleans, LA, The Cleveland Clinic Foundation, Cleveland, OH

Background: Beyond lipid-lowering, statins possess anti-inflammatory and anti-thrombotic effects. The relation between statin therapy and lowering of death/MI early after percutaneous coronary intervention (PCI) has been recently shown. We examined the inter-relationship of inflammation, statin use, and PCI outcome.

Methods: Within the year 2000, 1,552 consecutive patients underwent elective/urgent PCI at the Cleveland Clinic and were prospectively followed. Pre-procedural serum high-sensitivity C-reactive protein (CRP) levels were measured. Comparisons were made between patients with and without statin pretreatment.

Results: Statin-users (39.6%) had a lower median CRP level (0.40 mg/dl vs 0.50 mg/dl, P=0.012) independent of the baseline cholesterol levels, and had less incidence of periprocedural myocardial infarction (MI, 5.7% vs 8.1%, P=0.038). At 1 year, statin pretreatment was predictive of survival almost exclusively among patients within the highest CRP quartile (CRP >1.11 mg/dL) (Figure). In multivariate analysis, the interaction between CRP quartiles and statin use remained significant (P=0.014). After adjusting for the propensity of receiving statin, statin pretreatment was an independent predictor for 1-year survival within the highest CRP quartile (HR=0.44, P=0.039).

Conclusions: Statin therapy prior to PCI is associated with a marked survival benefit among patients with high CRP levels, suggesting mechanism tied to a particular anti-inflammatory effect.



11:45 a.m.

880FO-6 **Prophylactic Acetylcysteine Is Not Effective in Preventing Contrast-Induced Nephropathy Following Coronary Angiography**

J. Bradley Oldemeyer, Erica K. Cichowski, Richard L. Wurdeman, Kathleen A. Packard, W. Paul Biddle, Aryan N. Mooss, Creighton University Medical Center, Omaha, NE

Background: Contrast-Induced Nephropathy (CIN) is associated with significant morbidity and mortality following coronary angiography. Oral acetylcysteine at a dose of 600 mg every twelve hours has had inconsistent results in preventing CIN following contrast administration in previously published reports.

Methods: 96 patients with a creatinine clearance of 50 ml/min or less were randomized in a double blinded manner the evening prior to coronary angiography to receive four doses of acetylcysteine 1500 mg every twelve hours versus placebo. All patients received 1/2 normal saline at 1 ml/kg for 12 hours before and 12 hours after angiography. CIN was defined as an increase from the baseline serum creatinine (SC) at 48 hours by 25% or 0.5 mg/dl. Multivariate analysis was utilized to identify the incidence of CIN as well as the absolute change in SC at 48 hours.

Results: Baseline characteristics in the groups were similar, with a mean baseline SC of 1.64 mg/dl. CIN developed in 4 of 49 (8.2%) patients in the acetylcysteine group and 3 of 47 (6.4%) in the placebo group (p=0.74). Volume of contrast was similar between the two groups: 134 ml in the acetylcysteine group and 127 ml in the placebo group (p=0.63). The mean change in the SC from baseline and at 48 hours following contrast exposure was -0.01 mg/dl in the acetylcysteine group and -0.05 mg/dl in the placebo group (p=0.52). Multiple variables were analyzed with regards to mean change in SC at 48 hours. The only significant covariate was the volume of contrast dye delivered (p=0.03). There was no benefit of acetylcysteine on change in SC at 48 hours regardless of the severity of renal insufficiency. Acetylcysteine was tolerated as well as placebo.

Conclusion: Acetylcysteine does not appear to prevent CIN in patients with a creatinine clearance less than 50 mg/dl who are undergoing coronary angiography. The volume of dye delivered continues to be recognized as a potent factor in the deterioration of kidney function following angiography.