1078-19 **Effects of the QUADDS-QP2 Drug-Eluting Stent Extend Beyond the Targeted Area Into Adjacent Nonstented Zones: Results of the SCORE Trial**

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Background: The QUADDS-QP2 stent, a 316L stainless steel stent that delivers QP2 (an antiproliferative taxane derivative) from polymer sleeves, was shown to reduce restenosis (RS) compared to placebo in the SCORE trial (RS includes thrombosis cases). Whether high doses of QP2 (4000 ug), delivered through 5 high capacity polymer membranes, as used in SCORE have any impact on adjacent non-target areas is not known. Methods: We performed QCA on the first 260 randomized pts treated for de novo native lesions (134 bare metal vs 126 QP2 Stents). Follow-up QCA (MEDIS), available in 77% (N=202), was performed with systematic analysis of the QP2 stent area as well as 5mm proximal and distal adjacent non-stented segments. Results: Baseline lesion characteristics were similar in both groups, including ACC/AHA class >B1 (32%), mean vessel size (2.96mm), lesion length (11.8mm), and final results (final stent DS 5%). Follow-up restenosis was reduced by 72% within the QP2 stent, 67% proximal and 65% distal to the stent (see table). Conclusion: High dose QP2 delivered via a high capacity polymer on the QUEST stent demonstrated striking reductions in RS within the targeted stent zone, with equal effects extending at least 5mm proximally and distally beyond the confines of the target stent, likely representing elution of QP2 into adjacent non-stented vessel areas. Whether positive remodeling is the mechanism of luminal improvement at the edges will be determined by IVUS.

	QUADDS-QP2 N=99	QUEST N=103	p value
Restenosis Stent(%)	10.1%	36.9%	0.0001
FU Proximal Edge DS, %	24±21	35±24	0.0007
Restenosis Prox Edge %	9.3%	28.4%	0.0006
FU distal Edge DS, %	16±18	25±22	0.001
Restenosis Distal Edge (%)	5.2%	14.7%	0.0267

1078-20 **Comparison of a Novel Polymer (PLL-g-PEG) With Gold-Coated and Stainless Steel Stents for Prevention of Neointimal Hyperplasia**

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Background: Stent coating aims to reduce neointimal hyperplasia. The purpose of this study was to investigate the effect of a novel polymer (poly-L-lysine with polyethyleneglycol=PLL-g-PEG) on neointimal hyperplasia and to compare it with gold-coated and stainless steel stents in the porcine restenosis model.
Methods: Three different (NIR) stents were implanted each in a total of 13 pigs: (1) an uncoated, stainless steel stent (control=bare NIR stent), (2) a polymer-coated stent (PLL-g-PEG dip-coated on a bare NIR stent), and (3) a gold-coated stent (NIR Royal). Stents were randomly implanted into either the left anterior descending, left circumflex or right coronary artery. Stent length and diameter were 16 mm and 3.0 mm, respectively. Inflation pressure was adjusted to achieve a balloon-to-artery ratio of 1.1:1. Six weeks after implantation, animals were restudied by quantitative coronary angiography, and then stented arteries were examined by digital histomorphometry.
Results: At follow-up angiography, all stents were expanded and patent. Angiographic restenosis was 14±8% for the control, 9±7% for the polymer-coated and 21±9% for the gold-coated stents ($p<0.04$). Histologic examination showed no evidence of thrombus formation or inflammatory cells surrounding the stent struts. Quantitative histomorphometry revealed a significant decrease in luminal area for gold-coated stents (4.60±2.14 mm2) compared with the control (5.58±2.2 mm2) and polymer-coated stents (5.81±2.0 mm2, ANOVA $p<0.01$). Neointimal hyperplasia amounted to 2.54±0.83 mm2 in control, 2.17±0.81 mm2 in polymer-coated and 2.95±1.16 mm2 in gold-coated stents (ANOVA $p<0.001$). Histologic restenosis rate was 34±18% in control, 29±14% in polymer-coated, and 41±19% in gold-coated stents (ANOVA $p<0.003$).
Conclusions: Surface modifications of stainless steel stents by passive coatings modify the amount of neointimal proliferation in the porcine restenosis model. Polymer-coating with PLL-g-PEG significantly reduces neointimal proliferation, whereas gold enhances neointimal formation compared with stainless steel. Thus, stent coating with PLL-g-PEG may be beneficial for prevention of instent restenosis.

1078-21 **Dramatic Inhibition of Neointimal Proliferation by the Paclitaxel-Eluting Stents Showing Radiation-Like Results Without Radiation: Insights From the QCA Core Laboratory**

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Background: Even in the absence of clinically relevant restenosis, neointimal proliferation within the conventional metallic stent results in approximately 30% loss of lumen diameter achieved by the stent implantation. Preliminary data suggest that local drug delivery directly from the stent surface is effective in reducing the restenosis rate. We sought to determine if paclitaxel eluted from the stent surface could change the pattern of restenosis by significantly minimizing the in-stent proliferation and thus better preserving the post-procedural gain.
Methods: ASPECT was a dose-finding trial comparing restenosis in stents eluting paclitaxel to control (conventional stents) at 4 to 6 month follow-up. While both doses significantly reduced restenosis as compared to control, the higher dose was most effective without apparent differences in safety. Of 177 patients enrolled, 60 patients received high-dose paclitaxel-coated stents. By the analysis of the quantitative coronary angiography (QCA) data, we calculated the incidence of percent diameter stenosis of less than 5% at the follow-up, which would indicate extraordinary inhibition of neointimal growth.
Results: Of patients in the high dose paclitaxel-coated stent group, 98% had a percent diameter stenosis of less than 50% (i.e. no binary restenosis) at the follow-up. More notably, 46% patients presented at the follow-up with percent diameter stenosis of 5% or less, compared to only 9% in the control group ($p<.0001$). There were no late thrombotic events.
Conclusion: The paclitaxel-eluting stent is capable of extraordinary inhibition of neointimal proliferation. This inhibition most likely does not occur at the cost of impaired vessel healing and reendothelialization since it was not associated with late thrombotic events. This pattern of minimal neointimal stent "paving" is fundamentally different from the thicker rind of neointimal growth almost invariably induced by conventional metallic stents.

1078-22 **A Quantitative Assessment of Regional Changes in Lumen Diameter After Photodynamic Therapy With Motexafin Lutetium in Patients Undergoing Stent Implantation**

Jeffrey J. Popma, Nicholas Cox, Dennis Wahr, Howard Herrmann, Daniel I. Simon, Campbell D. Rogers, Paul Kramer, Wendy Shear, Kendrick Shunk, Alan Yeung, Ross Prpic, Daniel Adelman, Dean Kereiakes, *Brigham and Women's Hospital, Boston, Massachusetts.*

Background: Motexafin lutetium (MLu, Antrin® Injection) is a synthetic expanded porphyrin-photosensitizing agent that localizes in atheroma. Upon activation of MLu with intra-arterial 732 nm light, singlet oxygen is produced and apoptosis of inflammatory cells occurs. Preliminary data suggests a potential benefit of MLu for restenosis, but its effects at the light therapy edges are unknown. **Methods:** We quantitatively analyzed cineangiograms obtained from 58 patients who underwent stent placement and were enrolled in a phase I drug and light escalation study (Group I: MLu dose range: 0.05-4.0 mg/kg; light range: 100 J/cm-fiber; Group II: MLu dose 2.0-3.0 mg/kg; light range: 200-600 J/cm-fiber). Image frames were compared before (BL) and just after endovascular illumination, and 6 months (FU) later. Analysis zones included the stent, injured segment, lighted segment, vessel, and a 5 mm segment proximal and distal to the light source. **Results:** Reference diameters measured 5 mm proximal and distal to the light source did not change during FU (BL: 2.83 ± 0.45 mm; FU 2.83 ± 0.44 mm). Mean % stenosis at FU were 41.1% within the stent, 41.5% within the injured segment, 42.7% within the lighted segment, and 44.2% in the vessel. In-stent binary restenosis was 39.5% in Group I and 26.3% in Group II. Lumen changes at the proximal (0.17 ± 0.56 mm) or distal (0.04 ± 0.42mm) ends were not consistent with an "edge effect." **Conclusions:** Treatment with MLu in patients undergoing stent implantation resulted in no deleterious lumen changes at the edge of the treatment zone (i.e., no "edge effect"). Restenosis was primarily located within the axial stent length and indicated an early dose and light response in its effect on restenosis. Further analysis of the potential biologic activity of MLu on the lighted but uninjured atherosclerotic regions is ongoing.

POSTER SESSION

1079 Optimizing the Selection and Use of GPIIb/IIIa Agents

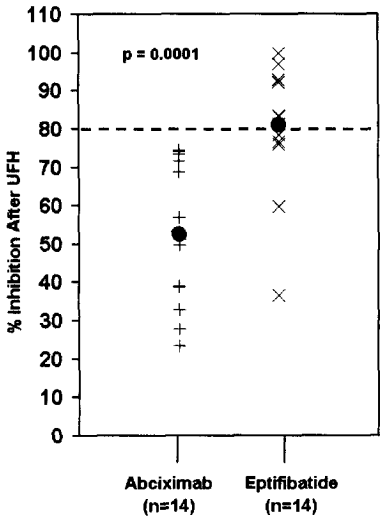
Monday, March 18, 2002, 9:00 a.m.-11:00 a.m.
Georgia World Congress Center, Hall G
Presentation Hour: 9:00 a.m.-10:00 a.m.

1079-6 **Unfractionated Heparin Reduces the Antiplatelet Effects of Abciximab but Not Eptifibatide During Coronary Interventions**

Efthymios N. Deliargyris, Laura G. Melton, Cheryl Thompson, Melrose Fisher, Don A. Gabriel, Gregory J. Dehmer, *University of North Carolina, Chapel Hill, North Carolina, Wake Forest University School of Medicine, Winston-Salem, North Carolina.*

Background: Abciximab (AB) and Eptifibatide (EP) are both effective during PCI, however only EP has proven beneficial as an adjuvant medical treatment for ACS. We hypothesized that the concomitant use of unfractionated heparin (UFH) may differentially effect the degree of platelet inhibition produced by AB and EP. **Methods:** In 28 pts undergoing PCI we obtained samples at baseline, 10 min after standard weight-based AB (n=14) or double-bolus EP (n=14) and 5 min after UFH (70 U/kg bolus). Percent inhibition of platelet aggregation was assessed after both weak (ADP) and strong (TRAP) platelet agonism and calculated based on the baseline values. All pts had received aspirin and 300 mg of clopidogrel. **Results:** Mean % inhibition was higher in EP pts compared with AB pts both before (96 vs 85% [ADP]; 89 vs 63% [TRAP], $p<0.001$ for both) and after UFH (96 vs 79% [ADP]; 81 vs 52% [TRAP], $p<0.001$). Addition of UFH significantly reduced platelet inhibition in AB pts (85 vs 79% [ADP]; 63 vs 52% [TRAP], $p<0.05$ for both) but not in EP pts (96 vs 96% [ADP]; 89 vs 81% [TRAP]; p=ns for both). Following addition of UFH none of AB pts compared with 57% of EP pts achieved the "optimal" >80% inhibition of platelet aggregation (Figure). **Conclusions:** With standard dosing, EP

achieved superior platelet inhibition before but especially after UFH compared with AB. The significant reduction in platelet inhibition in AB pts with the addition of UFH may provide insight to the lack of clinical benefit observed with the combination of AB and UFH in GUSTO IV ACS.



1079-7 Renal Insufficiency and Its Relation to Ischemic and Bleeding Outcomes With Tirofiban Versus Abciximab in the TARGET Trial

Peter B. Berger, David J. Moliterno, Jennifer White, Patricia J. Best, Albert W. Chan, Steen D. Kristensen, David R. Holmes, Jr., Peter M. DiBattiste, Howard C. Herrmann, Eric J. Topol, for the TARGET Investigators, *Mayo Clinic, Rochester, Minnesota, Cleveland Clinic, Cleveland, Ohio.*

Background: Chronic renal insufficiency (CRI) is associated with an increased risk of both ischemic and bleeding complications in patients (pts) undergoing percutaneous coronary intervention (PCI). Platelet glycoprotein (GP) IIb/IIIa inhibitors decrease ischemic complications but increase the risk of bleeding in PCI pts; the risk:benefit ratio of these agents, and whether it differs between agents that are renally excreted (tirofiban) or not (abciximab) is unknown. **Methods:** We analyzed the outcome of 4623 pts undergoing PCI in TARGET randomized to tirofiban or abciximab to determine the efficacy and risk of bleeding with varying degrees of CRI. Pts were grouped in quartiles based on estimated creatinine clearance (CrCl) (<70, 70-90, 90-114, >114 ml/min) using the Cockroft-Gault formula. **Results:** Increasing age, female gender, hypertension, prior CABG and stroke were associated with lower CrCl (p<0.001 all comparisons). Using unadjusted logistic regression tests for trend, the primary endpoint of 30-day death/MI/urgent TVR was significantly greater in pts with lower CrCl (7.3, 8.5, 5.1 and 5.8%, p=0.02), as were both major and minor bleeding complications (major: 1.6, 1.0, 0.4, 0.3%; minor: 5.3, 4.3, 2.4, 2.0%, p<0.001 for both comparisons). However, ischemic and bleeding complications were more common in both the tirofiban and abciximab pts with lower CrCl. There was no evidence of interaction between GP IIb/IIIa inhibitor used and CrCl levels with respect to ischemic outcome, major bleeding, or minor bleeding (p=0.48, p=0.99, and p=0.13, respectively). **Conclusions:** CRI is associated with increasing age, female gender, and hypertension, and an increased risk of both ischemic and bleeding complications in pts undergoing PCI, despite treatment with GP IIb/IIIa inhibitors. Although tirofiban is renally cleared and abciximab is not, there is no evidence of interaction between drug and CrCl with respect to ischemic or bleeding events.

1079-8 Influence of Prolonged Intracoronary Heparin Infusion on Early and Long-Term Clinical and Angiopgraphic Outcome in Patients Undergoing Primary Angioplasty for Acute Myocardial Infarction

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Aim of the present study was to evaluate whether primary PTCA for acute myocardial infarction (AMI) associated with prolonged intracoronary heparin infusion reduce the incidence of "no flow" phenomenon and improve clinical outcome in patients -pts- with acute myocardial infarction Methods: 106 consecutive pts (77 males, 29 females, aging 32 to 78 years) admitted with the diagnosis of AMI who underwent primary coronary angioplasty (PTCA). In 64 pts (Group A) primary PTCA was performed using an autoperfusion balloon catheter and prolonged inflations (mean inflation time = 3.7 hours) associated with intracoronary perfusion of heparin (1000 UI/hour) while 42 pts (Group B) underwent primary PTCA with conventional PTCA catheters and inflation duration (mean total infaltions time = 12 minutes) without adjunctive pharmacological therapy. Angigraphic control was performed in all pts at 24 hours and 6 months following the procedure. Results: immediate success was obtained in all pts of group A and in 41 pts of group B. One pts of the latter group died early after the procedure because of cardiogenic shock. Mean residual stenosis was similar iun both groups. "No flow" phenomenon was observed in 12 pts, despite an optimal angiographic patency on the infarct-realted artery; only 1 patient was of group A and the other 11 were from group B (1,6% vs 19%, p<0.01) Early reocclusion or reccurrent angina (within 24hours) occured in 4 pts ; 1 was of group A and 3 of group B (1.5 vs 6.2% p= 0.06). After a mean follow up of 24.7 months) 73 pts (49 from group A and 24 from group B, p<0.01) were symptoms- and event free. There were 4 cardiac deaths (2 in each group). Reccurent silent and symptomatic ischemia was present in 26 pts, 12 from group A and 14 from group B (18.7% vs 34.1%, p<0.05). At 6 months, angiographic restenosis was present in 38 pts (18 from group A and 18 from group B; 28 vs 43.9%, p<0.001). Conclusions: primary PTCA associated with prolonged heparin intracoronary infusion reduces "no flow" phenomenon after successful reperfusion improving immediate and long-term outcomes of the procedure These findings give an indirect evidence that microvascular function could play a crucial role on the outcome of reperfusion therapy in pts with AMI.

1079-9 Relationship of the Degree of Procedural Anticoagulation to Outcomes After Stent Implantation

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Background: The level of procedural anticoagulation (activated clotting time (ACT)) during *balloon angioplasty* is inversely related to short-term ischemic events. Whether such a relationship exists in pts undergoing stent implantation is unknown.
Methods: We studied the procedural and in-hospital outcomes of 1,020 consecutive pts receiving stents (from 1997 to 1999). Pts within 72 hours of acute MI, with thrombolytics or GPIIb/IIIa inhibitor therapy were excluded. Based on the maximal procedural ACT, patients were separated into tertiles (n=340 in each): (i) Lower, with ACT = 236 ± 31 (range 149-274); Middle, with ACT = 295 ± 11 (range 275-312) and Upper, with ACT = 353 ± 40 (range 313-538).
Results: Other than age (Table), baseline clinical characteristics and lesion morphology were similar among the groups.

Tertiles of ACT values:	Lower	Middle	Upper	P
Age (yrs)	64.1 ± 11.3	64.8 ± 11.4	66.6 ± 11.6	0.01
Procedural Heparin Dose (U)	10,595 ± 5,104	13,808 ± 5,440	13,330 ± 4,679	<0.0001
Angiographic Success (%)	99.7	99.7	100	0.55
Abrupt Closure (%)	0.0	0.3	0.6	0.66
No Reflow (%)	0.6	0.2	0.0	0.07
In-Hospital Events				
Death or Q-Wave MI (%)	0.6	0.3	0.9	0.88
Non Q-Wave MI (%)	9.9	14.1	18.9	0.01
TLR (%)	0.0	0.9	0.3	0.18
Vascular complications (%)	5.2	4.1	4.0	0.68
Blood transfusions (%)	7.4	4.5	6.4	0.27

Conclusions: In patients receiving stents without GP IIb/IIIa inhibitors, there is no evidence that a high level of procedural anticoagulation results in significantly improved angiographic or clinical outcomes. These data support an empiric strategy of reduced heparinization during stent implantation to minimize hemorrhagic risks.

1079-10 Tirofiban Decreases the Intensity of Creatine Kinase and Troponin I Release After Rotational Ablation

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The Rotational Atherectomy (PTCRA) procedure has been associated with post-procedure release of creatine kinase (CK). Abciximab (Reopro) has been shown to decrease the intensity of this release. We prospectively randomized 126 patients to receive Tirofiban {Aggrastat} (N=61) or placebo (N=65) during and after the PTCRA procedure. A sub group of 20 patients had a determination of platelet aggregation using the Array Medical platelet aggregometer, before and during the PTCRA procedure. There were no significant differences in the patient populations in regard to age, gender, indications for the procedure or lesion complexity. Sixteen patients were excluded from statistical anlaysis, (9 placebo, 7 Tirofiban) because of absence of pre-procedure data (N=3), or pre-procedure CK elevation (N=13). The frequency of complications was low for both groups (Tirofiban vs. control), CABG: 0% vs 0%, Q-wave MI: 0% vs 0%, death: 0% vs 0%, bleeding: 0% vs 1.5%. Results of platelet aggregometry, CK release and Troponin I release are as follows:

	% Plt. Act	CKMB			Troponin I		
	(Ave.)	CKMBRelease <2x	CKMBRelease 2x-5x	CKMBRelease >5x	TropRelease <2x	TropRelease 2-5x	TropReleas e >5
Tirofiban	14.9	48(98.0%)	1(2.0%)	0(0.0%)	37(86.0%)	5(11.6%)	1(2.3%)
Placebo	86.6	46(83.6%)	6(10.9%)	3(5.4%)	33(70.2%)	8(17.0%)	6(12.8%)
P value	0.001		0.036			0.062	

Conclusion: In this group of patients, Tirofiban reduces the intensity of CK and Troponin I release after the PTCRA procedure. The magnitude of this reduction is similar to that reported for Abciximab. In addition, the rotational ablation procedure appears to be an excellent test vehicle, in which to measure drug efficacy for ameliorating cardiac enzyme rise after coronary intervention. Tirofiban causes a significant reduction in platelet activity.