doses of clopidogrel were effective in presence of aspirin suggesting clopidogrel and aspirin may have synergistic effects in prevention of acute stent thrombosis.

991-46 Ticlopidine Attenuates Post-Stent Implantation Thrombin Generation

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Stent implantation (S) is a procedure that fractures and ablates the endothelium, consequently activates hemostasis. Ticlopidine (T) and Aspirin (ASA) are thought to protect patients (pts) undergoing dilatation from thrombus formation. Being unknown the level of intracoronary thrombin generation, in 35 pts undergoing S implantation for a 76 ± 2% stenosis we measured thrombin antithrombin complexes (TAT) and the prothrombin fragment 1 + 2 (F1 + 2) in blood withdrawn from a peripheral vein (Bas Vein) and the proximal coronary artery (Bas Art). Measurements were repeated soon after and 10 min after S + PTCA, collecting blood in the distal dilated vessel (Dist Art) through a 0.018-inch internal lumen probing catheter. All pts were pretreated with 250 mg/d ASA, 500 mg/d T, β-blockers, calcium-antagonists and nitrates. During dilatation 150 U/Kg iv heparin (H) and 3 + 3 mg isosorbidedinitrate (ISDN) were ic injected. Eighteen pts received ≤ 24 h T and 17 pts ≥ 72 h T. 17 pts had GT-Roubin and 18 had Palmaz-Schatz stent/s (Pal-Sch) implantation.

Results:

				Bas Vein	Bas Art	S + PTCA Dist Art	10 min Dist Art
TAT	R	≤ 24 h T	ng/ml	10.8±3	15±4.3	10.8±4	13.5±4.1
TAT	R	≥ 72 h T	ng/ml	3.0±0.2	2.9±0.2	3.6±0.6	2.9±0.2
TAT	P	≤ 24 h T	ng/ml	11.1±2.4	13.3±6	16.7±6	7.6±1.5
TAT	P	≥ 72 h T	ng/ml	3.0±0.3	2.6±0.2	2.9±0.1	2.7±0.1
F1 + 2	R	≤ 24 h T	nmol/L	1.6±0.1	2.9±0.5	1.9±0.4	2.4±0.7
F1 + 2	R	≥ 72 h T	nmol/L	1.0±0.2	1.0±0.2	1.0±0.2	0.9±0.3
F1 + 2	P	≤ 24 h T	nmol/L	1.4±0.2	2.4±0.9	2.2±0.8	1.6±0.4
F1 + 2	P	≥ 72 h T	nmol/L	0.9±0.1	0.8±0.1	0.8±0.1	0.8±0.1

R = Roubin; P = Palmaz-Schatz; mean ± Sem (Anova), *Significant contrast vs ≤ 24 h T

The intra-procedure thrombin generation did not increase vs normal controls venous values (TAT 2.41 ± 1.4 ng/ml, F1 + 2 1.1 ± 0.3 nmol/L) after S + PTCA in pts receiving ASA + ≥ 72 h T + H. Ca antagonists, ISDN, ASA, H and ≤ 24 h T did not completely attenuate thrombin generation. No significant differences in thrombin generation were found between pts in whom Roubin or Palmaz-Schatz stents were implanted.

Conclusions: Thrombin generation following S + PTCA is reduced in patients treated with combination of ASA and ≥ 72 h Ticlopidine. The combined use of ASA, H and ≥ 72 h T might effectively protect patients from thrombus formation.

991-47 Thrombin and Fibrin Activity in Patients Treated With Enoxaparin, Ticlopidine and Aspirin Versus the Conventional Coumadin Regimen After Elective Stenting: The *ENTICES* Trial

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Limited data are available comparing the impact of the various antithrombotic drug regimens on hemostatic markers of thrombosis in the setting of intracoronary stenting. A 120 patient multicenter trial was organized to determine which antithrombotic regimen was more effective in reducing thrombosis. Patients were randomized in a 2:1 fashion to enoxaparin, ticlopidine, and aspirin (ETA) or to warfarin, heparin, dextran, dipyridamole, and aspirin (WHDDA). Blood samples were obtained preprocedure (baseline) and 3 days postprocedure. The hematologic markers performed included fibrinopeptide A (FPA), thrombin-antithrombin III complex (TAT), prothrombin fragment (F1.2), D-Dimer (D-D), and platelet factor 4 (PF4). For quality assurance, a collected sample was defined as inadequate and excluded from analysis if the value of the FPA was > 8.0 μg/L. Results for the first 40 patients are summarized below and represent the change from baseline to day 3 post-procedure. Values are expressed as mean ± standard error.

	FPA ng/ml	TAT ng/ml	F1.2 μg/ml	D-D ηM/ml	PF4 IU/ml
ETA	−0.82 ± 0.64	−2.2 ± 0.54	−0.2 ± 0.07	−5.3 ± 10.6	+12.5 ± 7.0
WHDDA	−0.81 ± 0.53	−1.0 ± 0.64	−0.02 ± 0.05	+59.8 ± 8.4	+18.5 ± 15.4

Conclusion: An interim analysis suggests that the hematologic markers of thrombin and fibrin generation are suppressed to a greater extent by a treatment strategy consisting of enoxaparin, ticlopidine, and aspirin. At the completion of the trial, a final analysis and correlation between these markers and clinical outcomes will be performed.

991-48 Platelet IIb/IIIa Blockade With Integrelin: Atherectomy Patients

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The IMPACT-II trial compared placebo and high- and low-dose integrelin, a platelet IIb/IIIa inhibitor, in patients undergoing interventional procedures. Of 4,010 pts randomized, 819 underwent either directional atherectomy (DCA; 451, 11.2%) or Rotablator atherectomy (ROTA; 380, 9.5%). Although not risk-adjusted for baseline lesion characteristics, the composite 30-day endpoint (death, MI, urgent bypass, repeat angioplasty or stent) was higher in DCA than non-DCA pts (15% vs 10%, p = 0.002) and in ROTA than non-ROTA pts (15% vs 10%, p = 0.001).

	Placebo	Integrelin		P
		Low-Dose	High-Dose	
DCA pts				
Composite endpoint	16.1%	13.4%	15.2%	0.619
MI	11.9%	12.2%	13.1%	0.816
Urgent CABG	1.4%	0	<1%	0.213
ROTA pts				
Composite endpoint	19.9%	12.5%	12.4%	0.059
MI	14.5%	10.9%	10.7%	0.304
Urgent CABG	7.6%	1.6%	2.5%	0.010

Although not risk-adjusted, in this large-scale, randomized trial composite ischemic events were 50% higher in DCA and ROTA pts. Integrelin markedly suppressed these events in ROTA pts and had a modest effect in DCA pts.

991-49 Local Delivery of Tissue Factor Pathway Inhibitor (TFPI) Decreases Mural Thrombus Formation Induced by Balloon Angioplasty

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Tissue factor is the most potent activator of blood coagulation, and is believed to have a critical function in hemostasis and thrombosis. Tissue factor may also be implicated in thrombus formation when the vessel wall is injured during balloon angioplasty, and may thus play an important role in abrupt closure and restenosis following angioplasty.

Whether in vivo administration of a tissue factor pathway inhibitor (TFPI) locally at the site of arterial wall injury, could prevent platelet thrombus formation was studied in normal pigs that underwent carotid arterial injury by a balloon dilatation catheter (5 inflations at 6 atm pressure for 30 sec at 1 min interval), after which TFPI was delivered locally and intramurally at the site of angioplasty through the distal micropores of a Localmed infusion sleeve. The left carotid was treated with 0.2 μg/kg of TFPI, while the right carotid was treated with vehicle solution. Autologous ^{51}Cr-platelet (PLT) deposition was quantified at the site of deep arterial injury, and was reduced from 28.1 ± 5.0 × 10^6/cm^2 on the control artery (n = 7), to 14.5 ± 4.3, p = 0.06 (n = 10) on the TFPI treated side. Prothrombin time was not changed with TFPI administration.

Thus, local administration of tissue factor pathway inhibitor via the Localmed infusion sleeve is feasible, and is associated with a 48% decreased platelet thrombus formation at the site of deep arterial injury, suggesting that tissue factor may be implicated in the thrombotic response after balloon angioplasty. This may have important clinical implications in the prevention of abrupt closure and restenosis following PTCA.

991-50 Expression of p53, bFGF and TGF$_{\beta 1}$ in Atherectomy Biopsies

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Distribution of p53 was analysed using a monoclonal antibody against the epitope of the amino acid sequence 1–45 in 48 biopsies (25 restenoses) obtained at directional coronary atherectomy. The proliferation associated antigen Ki-67 (MIB 1), the contractile filaments (α-actin, desmin), matrix components collagen VI and the basement membrane components, collagen IV, MIB 1, bFGF and TGF$_{\beta 1}$ were analysed immunohistologically using