	LD+H	LD-H	HD+H	HD-H	H
	(n=372)	(n=364)	(n=367)	(n=387)	(n=731)
Death or MI	12.6%	14.7%	18.0%	14.7%	18%
	0.66 (0.46,0.94)	0.78 (0.55,1.11)	1.00 (0.72,1.39)	0.78 (0.56,1.10)	

Odds ratios on the death/MI composite of LD and HD vs control were 0.72(0.54,0.95) and 0.89(0.68,1.16), respectively. Lamifiban with and without H exerted a consistent effect in reducing clinical events at 6 months. The combination of LD+H had the best profile compared with standard therapy.

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Pronounced Reduction in Long-Term Ischemic Events With Platelet IIb/IIIa Antagonism Among Diabetics With Unstable Angina: PARAGON 6-Month Results

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Diabetic patients have heightened platelet aggregability and worse outcomes after acute coronary syndromes compared with non-diabetics. To discern the possible benefit of potent platelet IIb/IIIa antagonism (lamifiban) among diabetic patients with unstable angina, we prospectively collected data from the PARAGON trial. PARAGON, a randomized, double-blind, placebo-controlled, 2282-patient trial of lamifiban in unstable angina, included 412 patients with diabetes. All patients received aspirin and either IV lamifiban (1μ g/min or 5μ g/min) or placebo for 72 hours. Compared with non-diabetics, diabetics were older and had more risks for CAD. Lamifiban-treated diabetics had a 29% lower incidence of death or myocardial infarction than placebo at 30 days (11.0% vs. 15.4%). At 6 months, diabetic patients treated with placebo had the highest rate of death, myocardial infarction, or the composite (Table). This adverse composite event rate was reduced by 36% with lamifiban (26.2% vs. 16.7% , *p<0.01). Non-diabetics had lower event rates than diabetics, and experienced only minimal reduction in events with lamifiban. In contrast, diabetic patients with acute coronary syndromes derive a particularly pronounced long-term benefit with early platelet IIb/IIIa blockade.

6-Month Adverse Events

	Diabetes		No Diabetes	
	Placebo	Lamifiban	Placebo	Lamifiban
Death, %	14.6	9.2*	4.9	5.1
MI, %	18.5	10.6*	12.7	11.8
Death/MI, %	26.2	16.7*	15.4	14.1

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Enhanced Anti-Platelet Therapy is More Important Than Choice of Thrombolytic Agent in the Treatment of Myocardial Infarction

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Mortality in ST-elevation MI is lower in patients treated with thrombolytic therapy than in those who are not. A small but further reduction in mortality has been reported based on the lytic agent selected. To assess the incremental benefit of adjunctive anti-platelet therapy to that of the lytic agent selected, ST-segment recovery analysis parameters known to reflect speed and stabilityof patency and clinical outcome were reviewed from all 1,108 analyzable continuous 12-lead ST-segment recordings available from the PARDIGM (253), PRIME (189), IMPACT-AMI-I (122), DUCCS-II (38), TAMI-9 (253) and GUSTO-I (253) trials. All pts had <6 hr pain and ST elevation on initial ECG. There were 907 pts treated with tPA and 201 with SK/APSAC (SK); 254 were treated with either lamifiban or integrilin parenteral (PLT) and 854 received no PLT; all pts had ASA. ST-segment recovery endpoints analyzed blinded to treatment or outcome included: PEAK ST deviation during the monitoring period (uV); time from onset of lytics to STABLE ST recovery of >50% (min); % of pts with early ST recovery & re-elevation suggesting CYCLIC flow of the infarct artery; LATE ST re-elevation after >4 hrs of STABLE ST recovery; and re-elevation episodes (RE-ST), and ST AREA (uV-min) under the level vs. time trend curve. Results, as % or 50th (25th, 75th %ile) were:

Thus: 1) enhanced anti-PLT activity has a more profound influence on the physiology of acute MI than the choice of lytic agent, and 2) this influence appears to be more in the speed with which stable reperfusion occurs than in the elimination of late events.

Variable	PEAK ST	STABLE	CYCLIC	LATE	REST	AREA
PLT*	395 (230,665)	89 (33,155)	17%	11%	29%	4643 (0,9694)
No PLT*	482 (300,705)	128 (58,241)	32%	16%	47%	6050 (1287,12603)
SK+	475 (305,710)	126 (59,206)	31%	20%	47%	7165 (2012,13850)
tPA+	455 (269,700)	112 (41,215)	28%	14%	42%	4838 (531,11226)
*p-value	.002	<.001	<.001	.094	<.001	.005
+p-value	.166	.588	.363	.045	.219	.010

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Early coronary patency evaluation of a platelet glycoprotein receptor antagonist (abciximab) in primary PTCA: the GRAPE-pilot study

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The best treatment of acute myocardial infarction (AMI) is achieving early patency of the infarct related artery (IRA). The results of thrombolysis and primary PTCA are already known. There is hardly any information about the effect of platelet glycoprotein receptor antagonists on early patency in AMI. In the GRAPE (Glycoprotein Receptor Antagonist Patency Evaluation) pilot trial we studied 41 patients (pts) with < 6 hour AMI eligible for primary PTCA and with a total of 10 mm ST-segment elevation or more. At hospital admission all pts were given oral aspirin 160 mg and 5,000 U iv heparin together with a bolus of abciximab (ReoPro®) 0.25 mg/kg followed by a 12 hour infusion of 10 mcg/min. As soon as possible the pts were brought to the catheterisation lab to undergo angiography and, if necessary, primary PTCA. **Results:** Median time between abciximab bolus and first injection for angiography was 45 minutes (range 10-90). The culprit lesion was found to be the RCA in 17 pts, the RCX in 3 and the LAD in 21 pts. At first IRA injection there was a TIMI flow grade 3 in 12 (30%) pts. Two pts (5%) showed TIMI flow grade 2. In 27 (65%) pts the IRA was totally occluded (TIMI flow grade 0 and 1). **Conclusion:** These preliminary data suggest, that abciximab given early in patients with a large AMI eligible for primary PTCA can achieve IRA patency in a third of the pts.

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A Randomized, Placebo-Controlled Crossover Trial of ReoPro Alone or Combined with Low-Dose Plasminogen Activator for Coronary Reperfusion in Patients with Acute Myocardial Infarction: Preliminary Results

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We have previously observed rapid initiation of coronary flow by ReoPro without exogenous plasminogen activators (EPA) in patients (pts) with acute coronary occlusion. In an ongoing double-blind, placebo-controlled, crossover trial of ReoPro alone or in conjunction with low-dose Activase, 26 pts within 6 hr of onset of acute myocardial infarction (AMI) and ST segment elevation have received aspirin (325 mg PO) and heparin (70 Unit/kg bolus plus 7 Unit/kg/hr continuous infusion IV), followed by randomization to blinded ReoPro (0.25 mg/kg IV bolus) or placebo. The primary objective is to document infarct-related artery (IRA) patency within 60-90 min after ReoPro alone; the effect of adjunctive Activase on IRA patency is the secondary goal. Protocol: Angiography of the IRA is performed at 60-90 min (Angio # 1) after initial therapy, and pts then cross over to blinded ReoPro or placebo bolus, whichever was not initially given. Angio # 2 is performed 10 min later. Pts not achieving TIMI 3 flow are further randomized to blinded Activase (20 mg IV) or placebo bolus, and Angio # 3 performed 15 min later. Blinded results to date: Treatment was initiated 2.9± 1 (mean± SD) hr after onset, and Angio # 1 performed 49± 14 min after randomization. At the time when all pts have had ReoPro alone for 10-90 min (Angio # 2), IRA flow was TIMI 0 in 8 pts, TIMI 1 in 5 pts, TIMI 2 in 5 pts, and TIMI 3 in 8 pts. An additional 22 pts will be enrolled. **Conclusions:** In this first randomized trial of a selective platelet glycoprotein IIb/IIIa receptor antagonist for reperfusion, alone or with low-dose adjunctive EPA, preliminary angiographic data shows that 50% of pts had TIMI 2 or 3 flow after ReoPro treatment alone.

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Angiographic Results from Platelet Receptor Inhibition for Ischemic Syndrome Management in Patients with Documented Unstable Angina or Non-Q-wave MI (PRISM-Plus)

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The angiographic (angio) study in PRISM-Plus was designed to examine the effect of tirofiban (Tir), a non-peptide platelet GP IIb/IIIa receptor blocker, compared to heparin (Hep) on angio-detected intracoronary thrombus (THR). 1168 pts with documented unstable angina or non-Q-wave MI were randomized to Hep or to CTH and had angiography a mean of 65± 17 hrs (0-97) after the randomization. Culprit lesions were identified based on the ECG ischemic region and the details of coronary anatomy and analyzed by the Core Lab, blinded to treatment. THR was analyzed using the TIMI-THR grade: 0=absent, 1=possible, 2=small (<0.5 x normal lumen diameter (NLD) at the greatest dimension), 3= medium (0.5-1.5 x NLD), 4=large (>1.5 x NLD), 5=recent total occlusion. Flow past the culprit lesion was assessed using TIMI-flow grade. The primary and secondary angio endpoints were the % of pts with each grade of THR and TIMI flow past the culprit lesion. Results: For 580 pts in CTH, the % of pts in THR grade 0-5 were 58, 12, 12, 12, 2 and 4, but were 53, 12, 9, 17, 3 and 6 for 588 pts in Hep (p=0.02). The % of pts with TIMI-flow grade 3-0 were 82, 9, 1 and 8 in CTH, versus 74, 13, 2 and 11 in Hep (p=0.002). Conclusions: In PRISM-Plus, compared to Hep alone, the CTH significantly reduced the