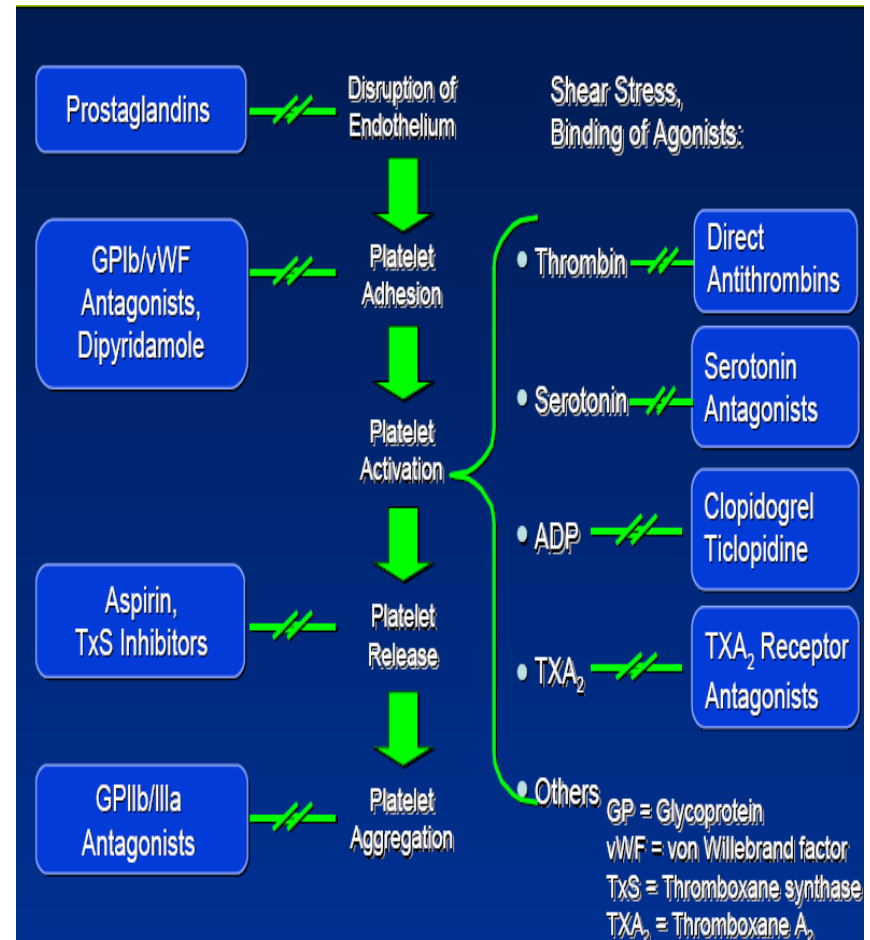
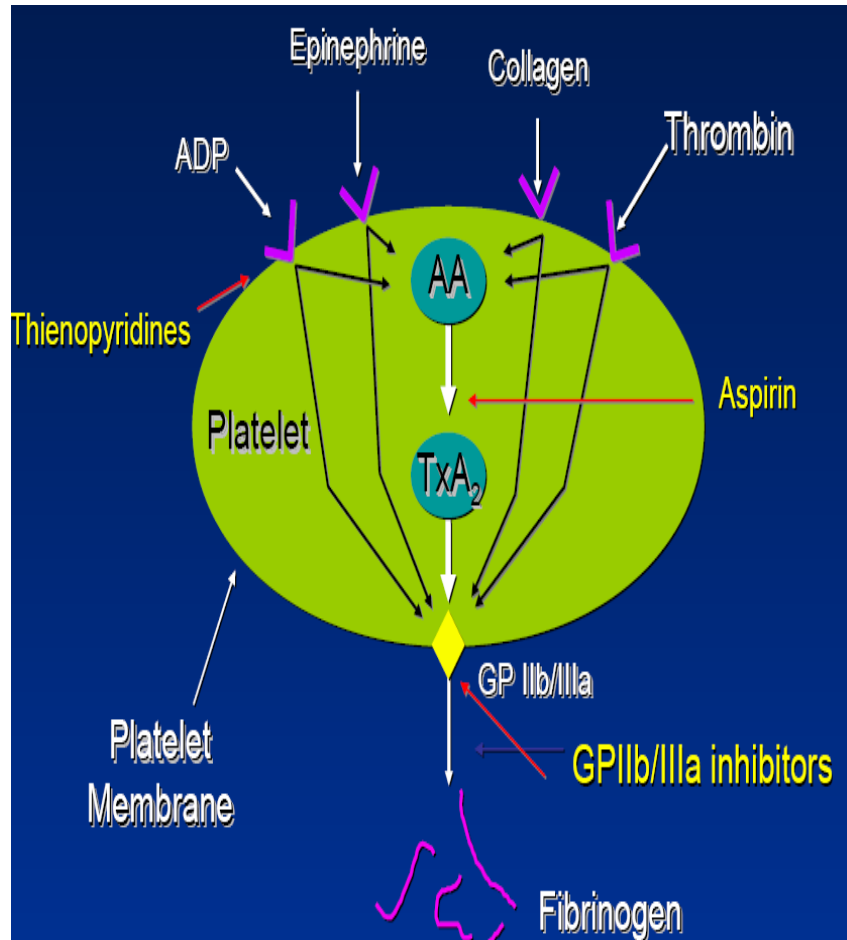


TRITHERAPIE ANTIPLAQUETTAIRE
et SCA :
prescription au cas /cas

APPAC BIARRITZ 2011

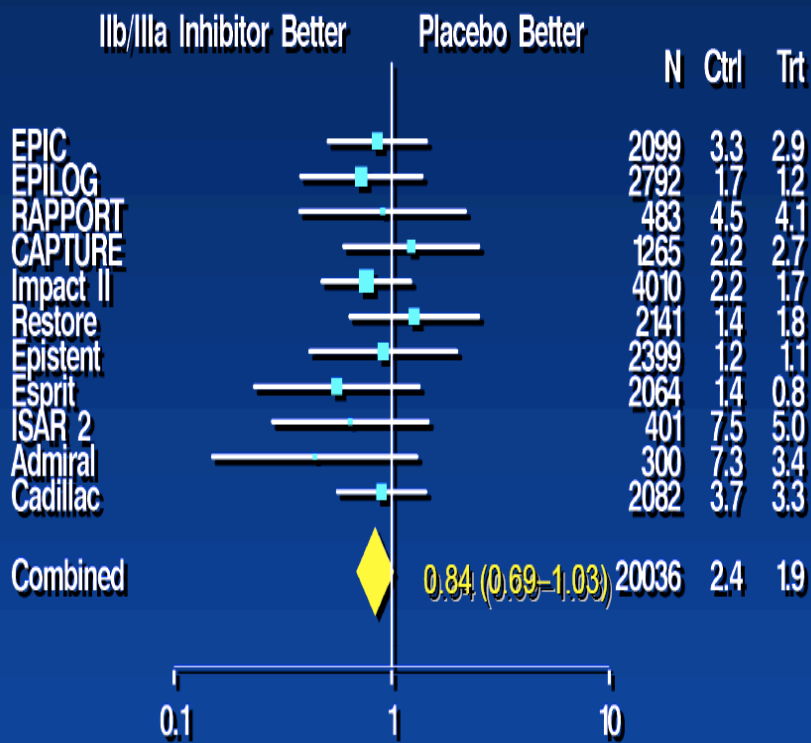
A.TIROUVANZIAM Institut thorax Nantes

Un probleme complexe pour le cardio interventionnel



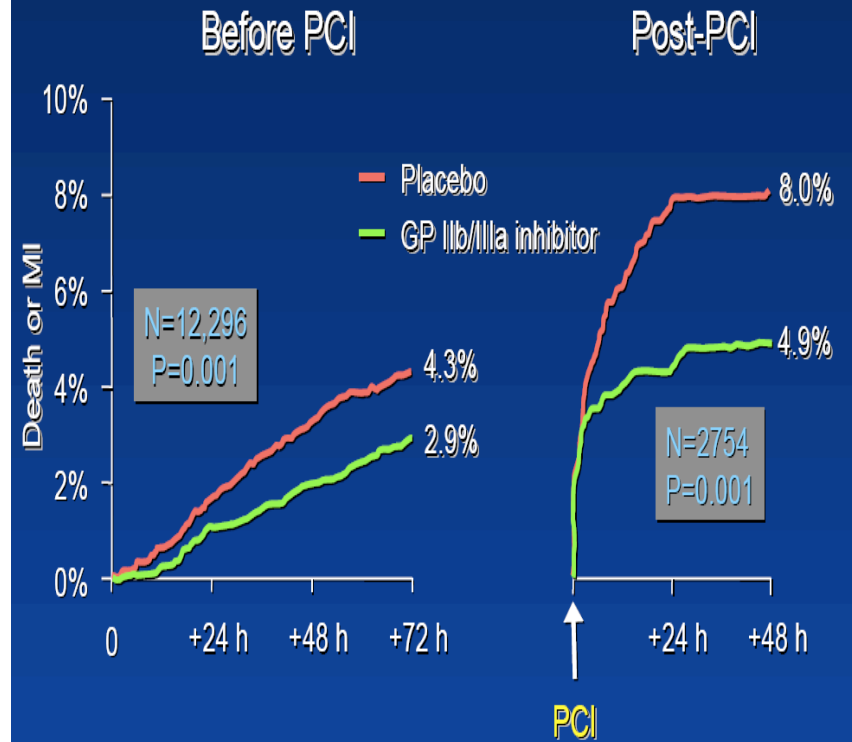
10 y 10 ans !

6-Month Mortality



Am J Cardiol 2003;92:651-5

CAPTURE, PURSUIT, PRISM-PLUS

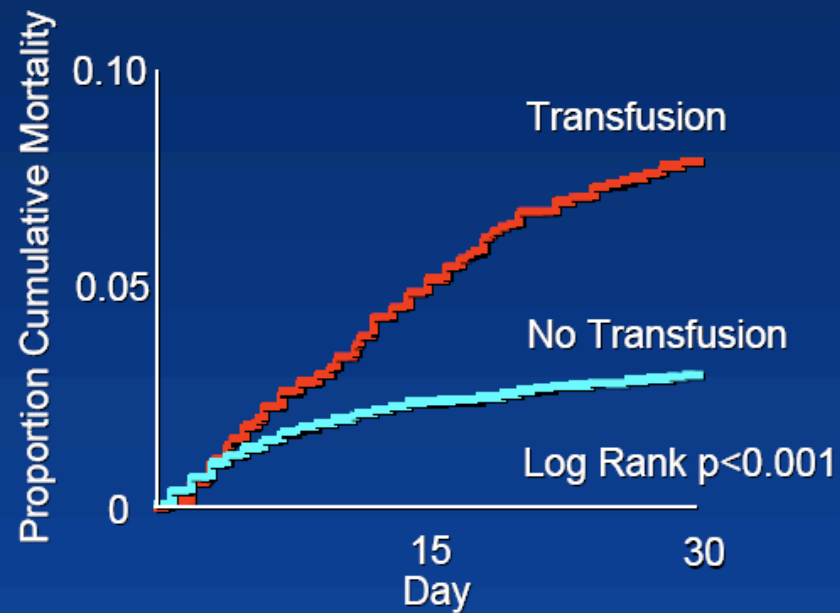
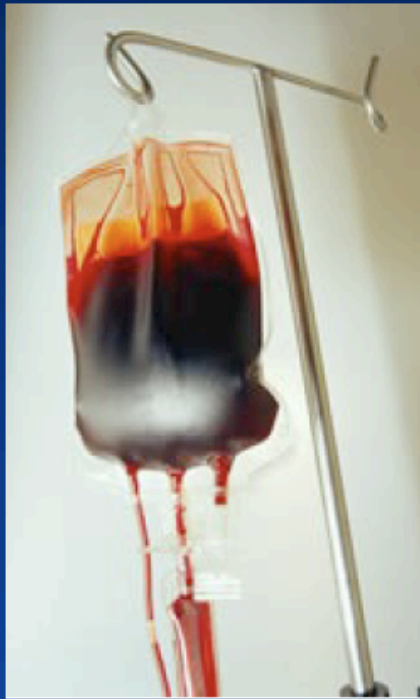


Boersma, Circulation, 1999

Le revers de la médaille!

Transfusion and 30-Day Mortality

24,112 patients from GUSTO IIb, PURSUIT, and PARAGON B



Rao, S. V. et al. JAMA 2004;292:1555-1562.

Depuis !!

Table 1 Major Recent Clinical Trials of Antiplatelet and Anticoagulants in NSTEMI-ACS

Trial	Agent	n	Primary Results	Note
NSTEMI-ACS				
ISAR-REACT 2 Kastrali et al. (7) JAMA 2006	GPI: abciximab vs. placebo	2,022	RRR of PE 25% at 30 days, p = 0.03 with sustained benefit at 1 yr p = 0.012	Benefit in patients with elevated cTn at 30 days and in all patients at 1 yr. Patients pre-treated with 600 mg of clopidogrel.
EVEREST Bolognese et al. (13) J Am Coll Cardiol 2006	GPI: upfront tirofiban vs. downstream GPI	93	TMPG 0/1 perfusion less frequent with upstream tirofiban vs. high-dose tirofiban or abciximab before PCI (28.1% vs. 66.7% vs. 71%, p = 0.0009)	Upstream tirofiban also associated with less frequent post-procedural cTnI elevation and lower cTnI levels after PCI
EARLY-ACS Giugliano et al. (14) N Engl J Med 2009	GPI: routine early vs. delayed provisional eptifibatid	9,492	No difference in PE (9.3% vs. 10.0%, p = 0.23) between early routine and delayed provisional groups	Trend toward fewer death/MI at 30 days (11.2% vs. 12.3%, p = 0.08), but more bleeding and transfusion with early routine eptifibatid.
ACUITY Stone et al. (9) N Engl J Med 2006	DTI: bivalirudin vs. bivalirudin and GPI vs. heparin and GPI	13,819	Bivalirudin alone noninferior for composite Ischemic EP (7.8% vs. 7.3%, p = 0.32), reduced major bleeding (3.0% vs. 5.7%, p < 0.001) and net clinical outcome (10.1% vs. 11.7%, p = 0.02)	ACUITY Timing trial (10) showed more composite Ischemic events with deferred GPI (7.9% vs. 7.1%, p = 0.13 superiority), which did not satisfy noninferiority
CURE Yusuf et al. (22) N Engl J Med 2001	Thienopyridine: clopidogrel vs. placebo	12,562	Reduced composite end point with clopidogrel (9.3% vs. 11.4%, p < 0.001)	Significantly more major bleeding with clopidogrel compared to placebo (3.7% vs. 2.7%, RR: 1.38, p = 0.001)
SYNERGY Ferguson et al. (63) JAMA 2004	LMWH: enoxaparin vs. UFH	10,027	No significant difference in PE with enoxaparin (14% vs. 14.5%, p = 0.40)	Significant increase in TIMI major bleeding with enoxaparin (9.1% vs. 7.6%, p = 0.008)
OASIS-5 Yusuf et al. (85) N Engl J Med 2006	LMWH: fondaparinux vs. enoxaparin	20,078	Fondaparinux noninferior in PE (5.8% vs. 5.7% p = 0.007 noninferiority)	Reduced major bleeding with fondaparinux (2.2% vs. 4.1%, p < 0.001)
STEMI				
FINESSSE Ellis et al. (16) N Engl J Med 2008	GPI: ± fibrinolytic Abciximab ± half dose of reteplase vs. placebo	2,425	No difference in PE with combination (GPI and fibrinolytic) or GPI vs. placebo (9.8% vs. 10.5% vs. 10.7%, p = 0.55)	Non ICH TIMI major bleeding through discharge greater with combination (GPI and fibrinolytic) (14.5% vs. 10.1% vs. 6.9%, p < 0.05)
On-TIME 2 Van't Hof et al. (17) Lancet 2008	GPI: high-dose tirofiban vs. placebo before PCI	984	Significantly lower extent of mean ST-segment deviation after PCI with tirofiban (3.6 mm vs. 4.8 mm, p = 0.003)	On background of clopidogrel 600 mg
HORIZONS-AMI Stone et al. (78) N Engl J Med 2008	DTI: bivalirudin vs. UFH and GPI	3,602	Primary composite of Ischemia and bleeding reduced with bivalirudin (9.2% vs. 12.1%, p = 0.005)	Reduction in bleeding with bivalirudin (4.9% vs. 8.3%), but increase in stent thrombosis (1.3% vs. 0.3%), both p < 0.001
CLARITY-TIMI 28 Sabatine et al. (24) N Engl J Med 2005	Thienopyridine: clopidogrel vs. placebo in patients planned for fibrinolytic	3,491	Significant reduction in PE with clopidogrel vs. placebo (15% vs. 21.7%, p < 0.001)	Similar rates of major bleeding and intracranial hemorrhage between the 2 groups
COMMIT/CCS-2 Chen et al. (25) Lancet 2005	Thienopyridine: clopidogrel vs. placebo	45,852	Significant reduction in PE with clopidogrel vs. placebo (9.2% vs. 10.1%, p = 0.002)	No significant increase bleeding (fatal, transfused, ICH) with clopidogrel
EXTRACT-TIMI 25 Antman et al. (68) N Engl J Med 2006	LMWH: enoxaparin vs. UFH in patients planned for fibrinolytic	20,506	Significant reduction in PE with enoxaparin vs. UFH (9.9% vs. 12.0%, p < 0.001)	Enoxaparin group was treated throughout the hospitalization. UFH group was treated for 48 h. Increased major bleeding was observed with enoxaparin (2.1% vs. 1.4%, p < 0.001).
OASIS-6 Yusuf et al. (86) N Engl J Med 2006	LMWH: fondaparinux vs. UFH or placebo	12,092	PE reduced with fondaparinux in total trial population (9.7% vs. 11.2%, p = 0.008)	Reduction in PE seen in Stratum I (no indication for UFH, randomized to fondaparinux or placebo), but not in Stratum II. Increased rate of catheter thrombosis in PCI group (n = 0 vs. 22, p < 0.001).
Across the spectrum of ACS (NSTEMI-ACS and STEMI)				
TRITON-TIMI 35 Wiviott et al. (43) N Engl J Med 2007	Thienopyridine: prasugrel vs. clopidogrel	13,608	Significant reduction in PE with prasugrel vs. clopidogrel (9.9% vs. 12.1%, p < 0.001)	More major bleeding with prasugrel (2.4% vs. 1.8%, p = 0.03)

Les guidelines ACC - AHA / ESC

Medical Management	
ACC/AHA (1-3)	ESC (4-6)
Class IIb (abciximab with half-dose lytic) Patients age <75 yrs	Class III
Class I (if subsequent recurrent symptoms/ischemia, heart failure, or serious arrhythmia occur angiography should be performed with upstream administration of either clopidogrel or GPI) Class IIa (if recurrent ischemic discomfort with clopidogrel, it is reasonable to add a GP IIb/IIIa antagonist before angiography) Class IIb (may be reasonable to add GPI to oral antiplatelet and anticoagulant therapy)	Class II (high risk)

	Early Invasive/PCI	
	ACC/AHA (1-3)	ESC (4-6)
STEMI (2,6)	Class IIa (abciximab) Class IIb (tirofiban, eptifibatide)	Class I (without stenting) Class IIa (with stenting)
UA/NSTEMI (1,3-5)	Class I (either GPI or clopidogrel in addition to aspirin should be initiated before angiography) Class IIa (reasonable to initiate antiplatelet therapy with both GPI and clopidogrel)	Class I (high risk)

1 - SCA non ST+



European Heart Journal (2010) 31, 2501–2555

doi:10.1093/eurheartj/ehq277

EUROPEAN SOCIETY OF CARDIOLOGY

ESC/EACTS GUIDELINES



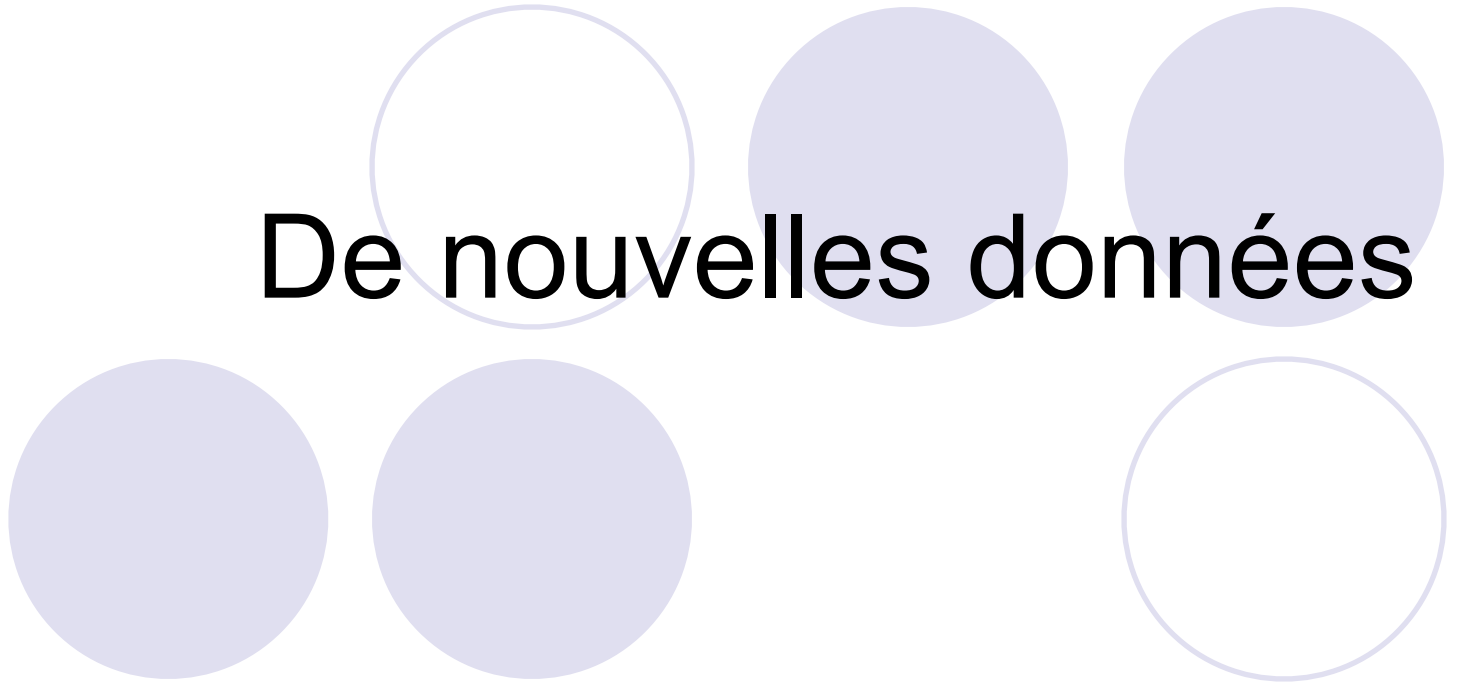
Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Developed with the special contribution of the European Association for Percutaneous Cardiovascular Interventions (EAPCI)[†]

NSTEMI-ACS				
Antiplatelet therapy				
	ASA	I	C	—
	Clopidogrel (with 600 mg loading dose as soon as possible)	I	C	—
	Clopidogrel (for 9–12 months after PCI)	I	B	55
	Prasugrel [‡]	IIa	B	246,247
	Ticagrelor [‡]	I	B	248
	* GPIIb/IIIa antagonists (in patients with evidence of high intracoronary thrombus burden)			
	Abciximab (with DAPT)	I	B	249
	Tirofiban, Eptifibatid	IIa	B	55
	Upstream GPIIb/IIIa antagonists	III	B	65
Anticoagulation				
Very high-risk of ischaemia [§]	UFH (+GPIIb/IIIa antagonists) or Bivalirudin (monotherapy)	I	C	—
	Bivalirudin (monotherapy)	I	B	251
Medium-to-high-risk of ischaemia [§]	UFH	I	C	—
	Bivalirudin	I	B	251
	Fondaparinux	I	B	250
	Enoxaparin	IIa	B	55,60
Low-risk of ischaemia [§]	Fondaparinux	I	B	250
	Enoxaparin	IIa	B	55,60

De nouvelles données



SCA non ST+

GPI: routine early vs.
delayed provisional
eptifibatide

EARLY ACS

~~EARLY ACS~~

Study Design

2 of 3 high-risk criteria:

1. Age \geq 60 years
 2. + CKMB or TnT/I
 3. ST \downarrow or transient ST \uparrow
- (Or age 50-59, h/o CVD
and + CKMB or TnT/I)

High-risk NSTE ACS

n = 10,500 (9500)

Early, routine
eptifibatide (180/2/180)

Placebo / provisional
eptifibatide pre-PCI

Randomize within 12 hours of presentation

Invasive strategy: 12 to 96 hours after randomization

1° Endpoint: 96-hr Death/MI/Urgent Revasc/Thrombotic bailout

2° Endpoint: 30-d Death/MI

Fade in safety endpoints at 120 hours (bleeding (GUSTO and TIMI scales), transfusions, stroke, non-hemorrhagic SAEs)

SCA non ST+

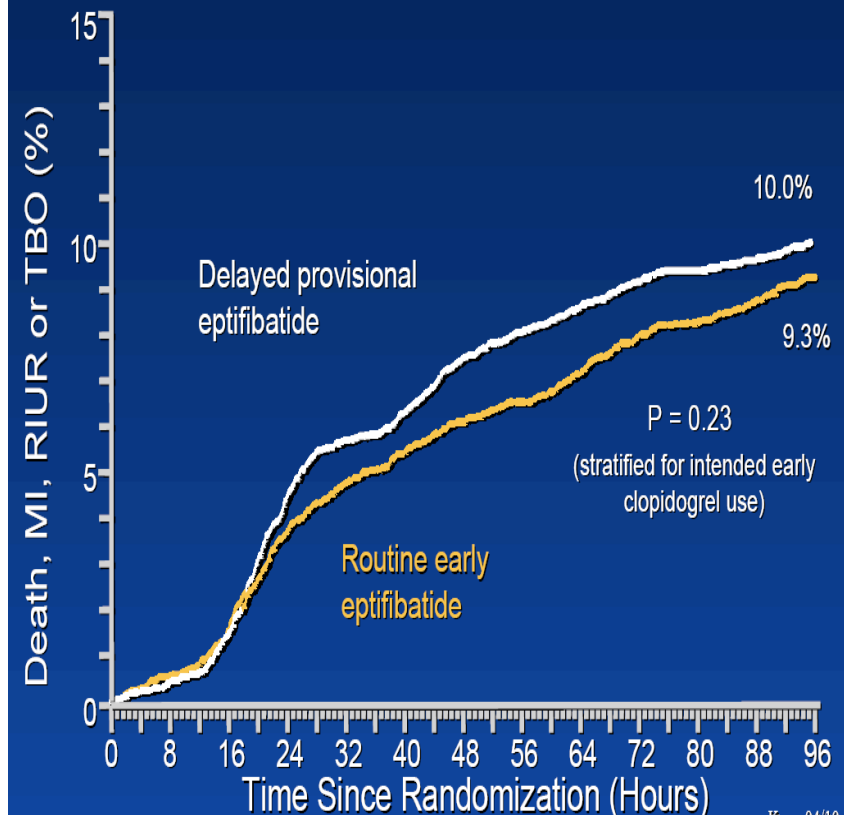
GPI: routine early vs. delayed provisional eptifibatide

EARLY ACS

96-Hour Primary Efficacy Results

	Routine Early Eptifibatide (n=4722)	Delayed Provisional Eptifibatide (n=4684)	OR (95% CI)	P
Death, MI, RIUR, TBO	9.3%	10.0%	0.92 (0.80-1.06)	0.23
Death	0.8%	0.9%	0.96 (0.62-1.50)	0.87
Death or MI	7.5%	8.3%	0.89 (0.77-1.04)	0.13
Death, MI, RIUR	8.4%	9.4%	0.89 (0.77-1.03)	0.11

Kaplan-Meier Curves for Primary Endpoint



SCA non ST+

GPI: routine early vs. delayed provisional eptifibatide

EARLY ACS

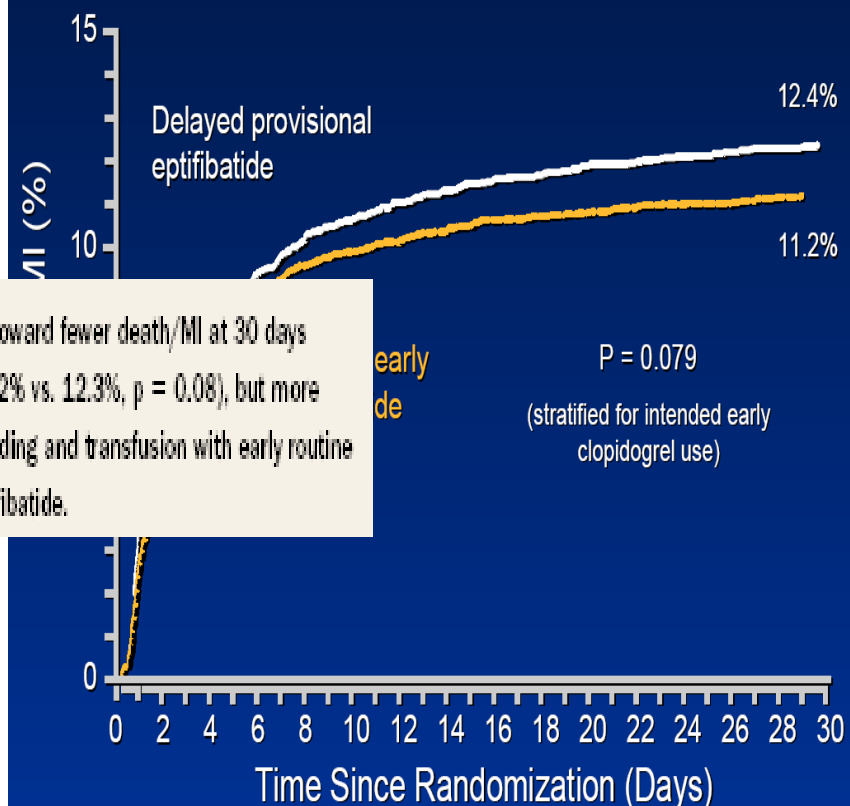
30-Day Secondary Efficacy Results

	Routine Early Eptifibatide (n=4722)	Delayed Provisional Eptifibatide (n=4684)	OR (95% CI)	P
Death or MI	11.2%	12.3%	0.89 (0.86-1.41)	0.079
Death	2.8%	2.8%		
Death, MI, RIUR	12.5%	13.8%	0.89 (0.79-1.01)	0.065

No difference in PE (9.3% vs. 10.0%, $p = 0.23$) between early routine and delayed provisional groups

Trend toward fewer death/MI at 30 days (11.2% vs. 12.3%, $p = 0.08$), but more bleeding and transfusion with early routine eptifibatide.

Kaplan-Meier Curves for 30-day Death or MI



Intracoronary Stenting and Antithrombotic Regimen—Rapid Early Action for Coronary Treatment (ISAR-REACT)-2

- **2,022** patients within 48 h **high-risk** UA/NSTEMI
- ASA + clopidogrel + abciximab vs ASA + clopidogrel
- **600 mg LD clopidogrel** ≥ 2 h before PCI → abciximab or placebo
- **↓ Death, MI, or urgent TVR by 30 d with abciximab**
 - ↓ if cTnT +; no diff if cTnT -
- **No diff major/minor bleeding**
- **Recommend: GP IIb/IIIa + clopidogrel if inv strategy used and high risk.**

Kastrati A, et al. JAMA 2006;295:1531-8.
LD = loading dose; LOE = level of evidence.

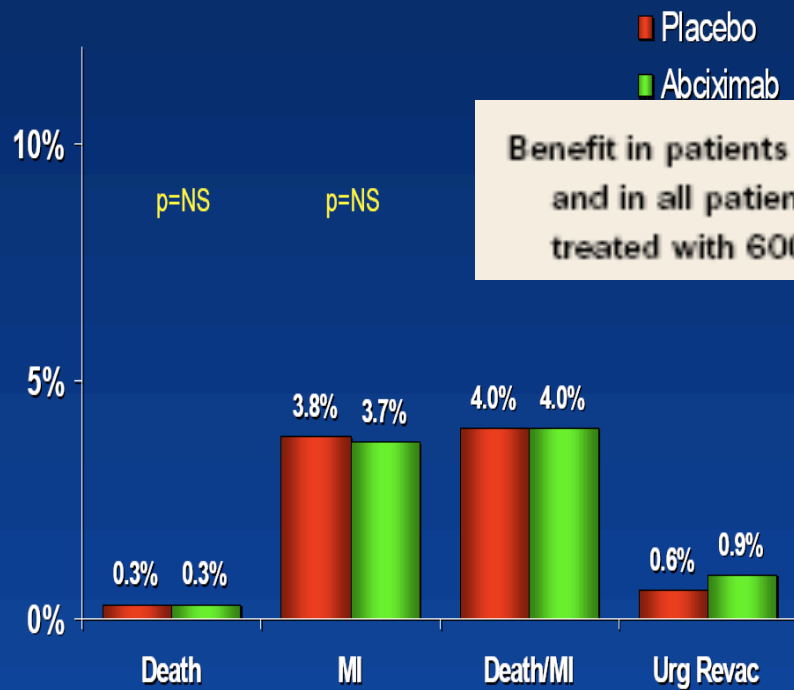
SCA non ST+

GPI: abciximab vs. placebo

ISAR REACT 2

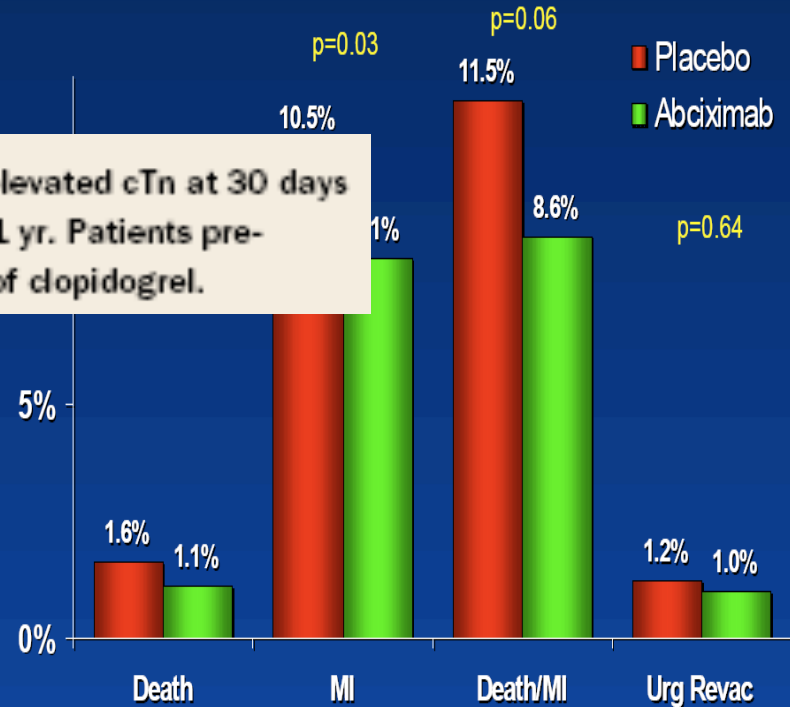
ISAR-REACT

Low-risk Patients – 30 Days



ISAR-REACT 2

Higher-risk Patients – 30 Days



Benefit in patients with elevated cTn at 30 days and in all patients at 1 yr. Patients pre-treated with 600 mg of clopidogrel.

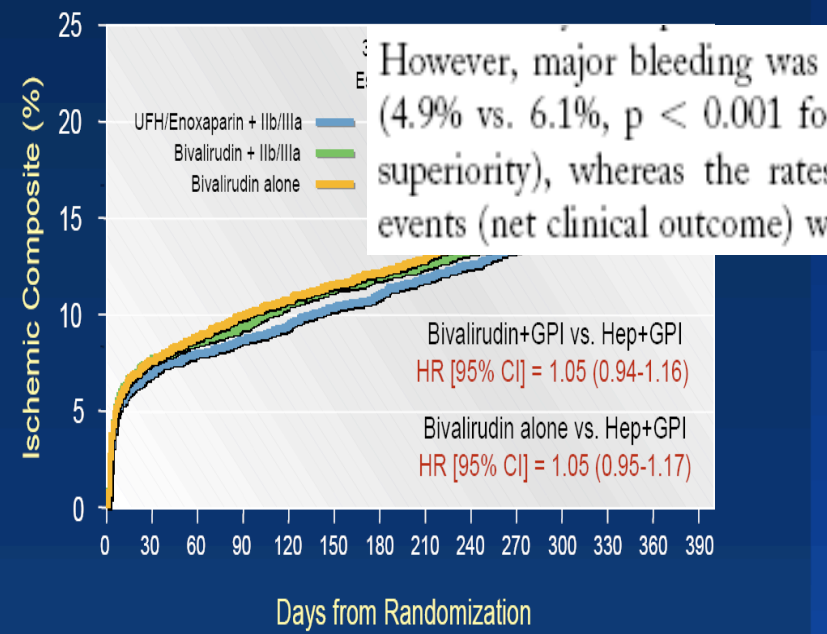
SCA non ST+: n= 13800 , +/- high risk , coro 72h, ss gpes early vs late GPI

DTI: bivalirudin vs. bivalirudin and GPI vs. heparin and GPI



ACUITY: Ischemic Composite Endpoint (Death, MI, unplanned revascularization for ischemia)

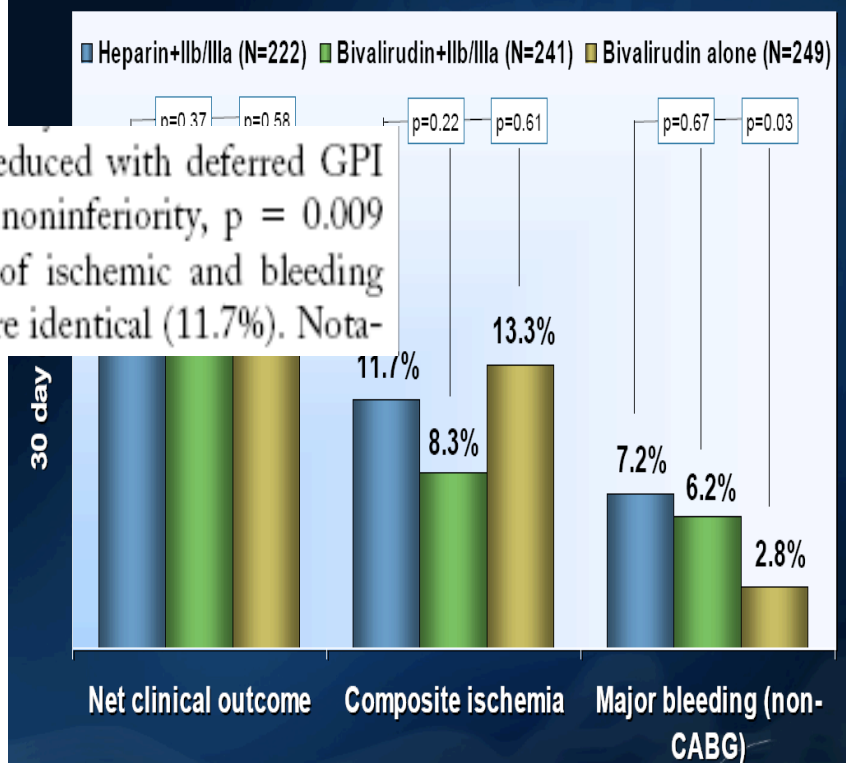
JFH/Enoxaparin + GPI vs. Bivalirudin + GPI vs. Bivalirudin Alone



However, major bleeding was reduced with deferred GPI (4.9% vs. 6.1%, $p < 0.001$ for noninferiority, $p = 0.009$ superiority), whereas the rates of ischemic and bleeding events (net clinical outcome) were identical (11.7%).

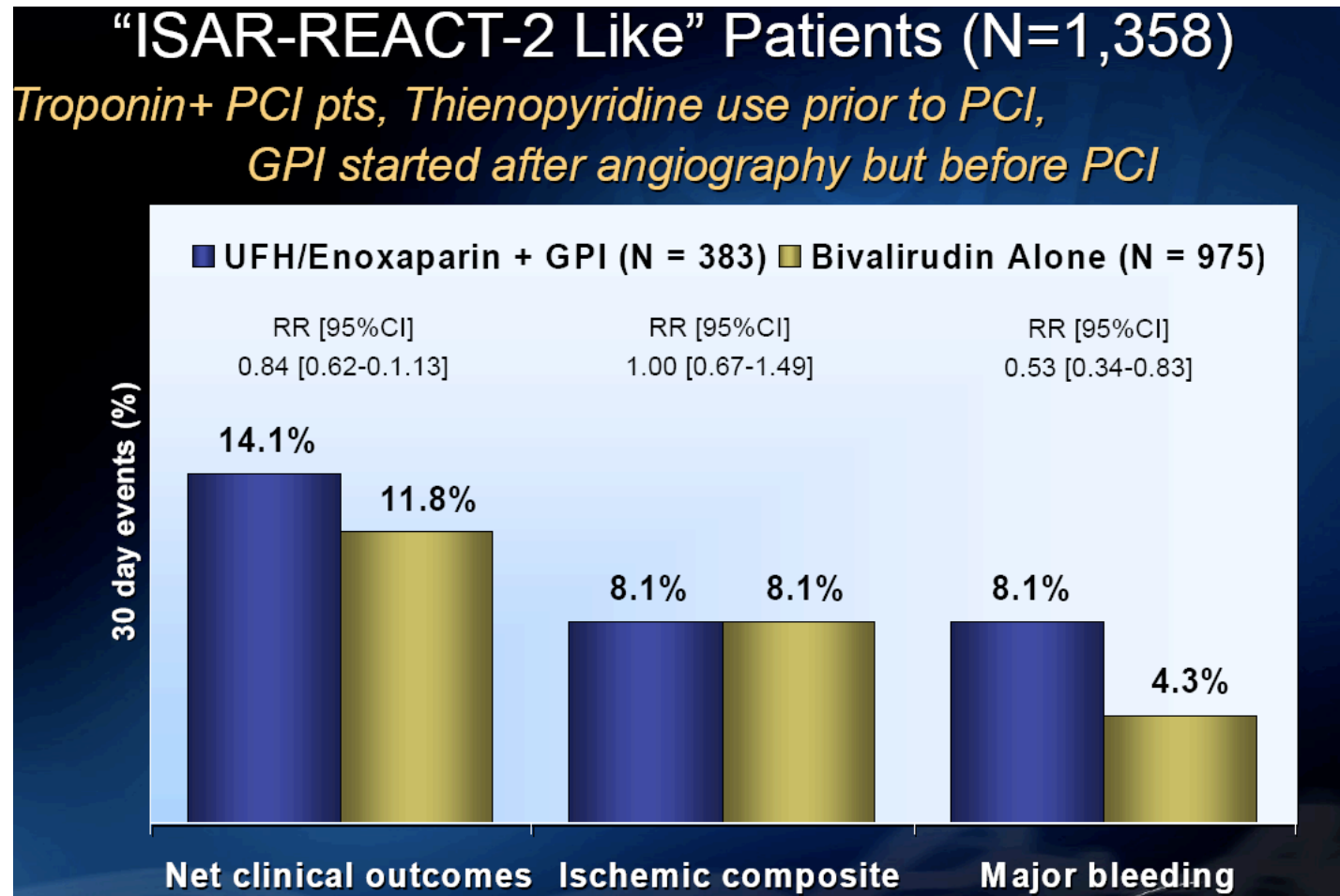
Primary Endpoint Measures

Patients with ≥ 1 PCI Thrombotic Lesion at Baseline (n=712)



Stone et al. (9)
N Engl J Med 2006

SCA non ST+

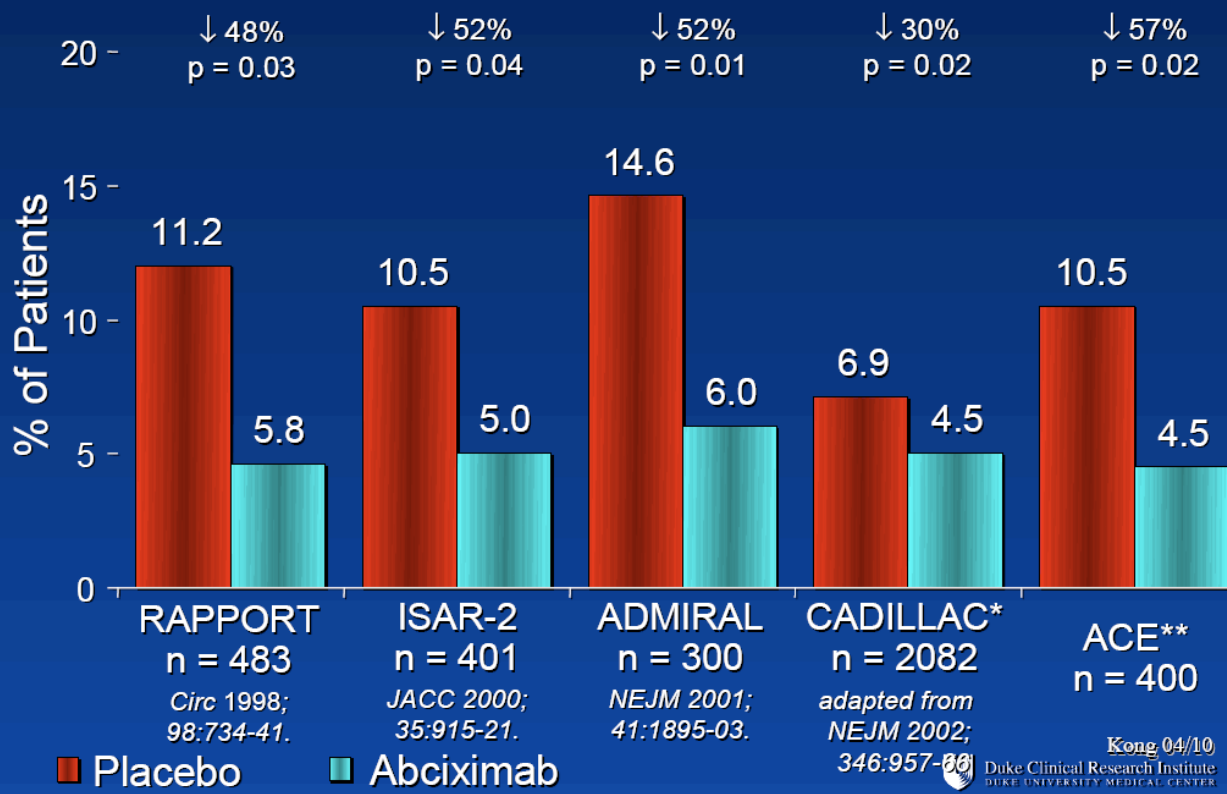


SCA non ST+ études %PCI

- ACUITY 55%
- EARLY ACS 60%
- TIMACS 55- 60%
- ICTUS 60%

2- SCA ST+

Primary PCI 30 Day Death, MI or Urgent TVR



Les guidelines

STEMI				
Antiplatelet therapy				
	ASA	I	B	55, 94
	Clopidogrel ^d (with 600 mg loading dose as soon as possible)	I	C	—
	Prasugrel ^d	I	B	246, 252
	Ticagrelor ^d	I	B	248, 253
	+ GPIIb/IIIa antagonists (in patients with evidence of high intracoronary thrombus burden)			
	Abciximab	IIa	A	55, 94
	Eptifibatid	IIa	B	259, 260
	Tirofiban	IIIb	B	55, 94
	Upstream GPIIb/IIIa antagonists	III	D	80
Anticoagulation				
	Bivalirudin (monotherapy)	I	B	255
	UFH	I	C	—
	Fondaparinux	III	B	256

SCA ST+



ClinicalTrials.gov Identifier: NCT00133250

Abciximab in Patients with AMI Undergoing Primary PCI After Clopidogrel Pretreatment

BRAVE-3 Trial

Bavarian Reperfusion Alternatives Evaluation-3 Trial

J. Mehilli, A. Kastrati, K. Huber, S. Schulz, J. Pache,
C. Markwardt, S. Kufner, F. Dotzer, K. Schlotterbeck,
J. Dirschinger, A. Schömig

SCA ST+

BRACE-3

Inclusion Criteria

- Patients with acute ST-elevation myocardial infarction presenting within 24 hours from the onset of symptoms
 - chest pain lasting more than 20 min
 - ≥ 0.1 mV of ST-segment elevation in ≥ 2 limb leads or ≥ 0.2 mV in ≥ 2 contiguous precordial leads or new left bundle branch block on surface ECG
- Written, informed consent

BRACE-3

Study Therapy

(randomized, double-blind)

Clopidogrel 600 mg oral
Aspirin 500 mg i.v. or oral
Unfractionated Heparin 5000 IU

Abciximab

n=401

Bolus: 0.25 mg/kg
Infusion: 0.125 μ g/kg/min/12h

Placebo

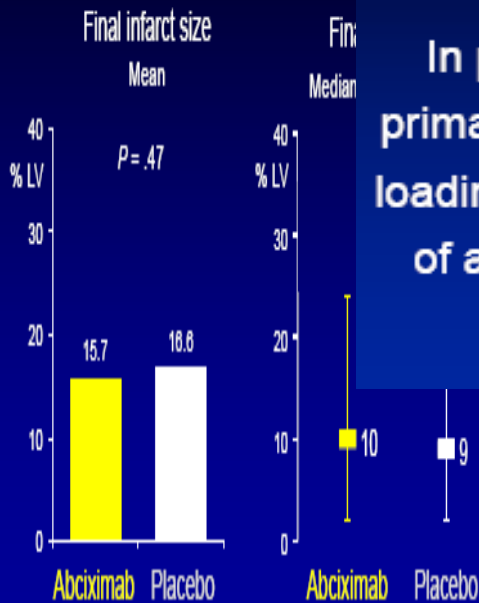
n=399

Additional UFH bolus of 70U/kg
Placebo infusion for 12h

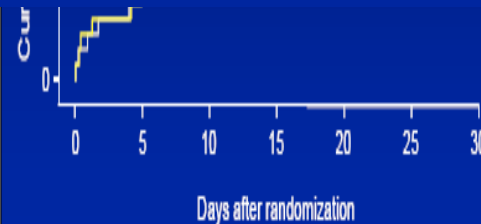
Aspirin 200mg/day indefinitely
Clopidogrel 2 x 75mg/day for 3 days
Clopidogrel 75mg/day for at least 4 weeks

SCA ST+

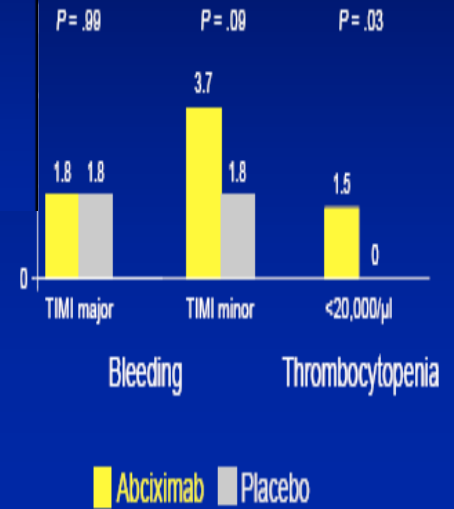
Primary Endpoint



30-Day Mortality



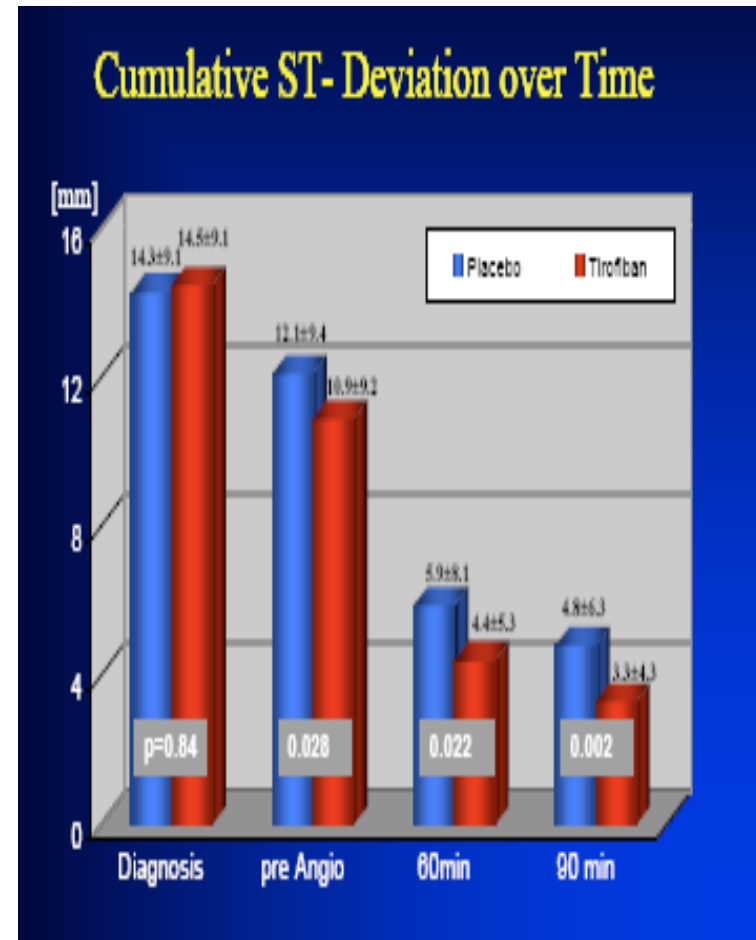
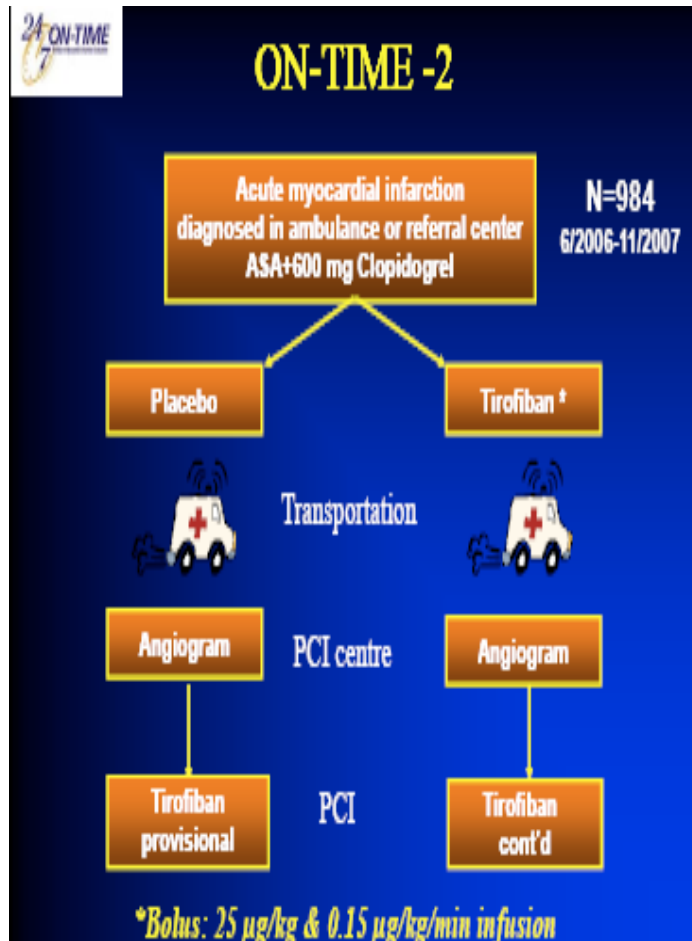
Clinical Adverse Events - 30 days -



In patients with acute STEMI undergoing primary PCI after pre-treatment with a 600mg loading dose of clopidogrel, the additional use of abciximab is not associated with further reduction in infarct size

SCA ST+

GPI: high-dose tirofiban vs. placebo before PCI



Van't Hof et al.
Lancet 2008

SCA ST+

Clinical Secondary Endpoints: 30 days

	Placebo n=477	Tirofiban n=473	p-value
Death	19 (4.0%)	11 (2.3%)	0.144
Recurrent MI	14 (2.9%)	10 (2.1%)	0.363
Stroke	7 (1.5%)	6 (1.3%)	0.41
Urgent TVR	23 (4.8%)	19 (4.0%)	0.546
Death/MI/TVR/Stroke	47 (9.9%)	34 (7.2%)	0.141
Thromb. Ball out	140 (28.5%)	97 (19.9%)	0.002
Combined	159 (33.3%)	123 (26.0%)	0.013

Significantly lower extent of mean ST-segment deviation after PCI with tirofiban (3.6 mm vs. 4.8 mm, $p = 0.003$)

Safety Endpoint: Bleeding

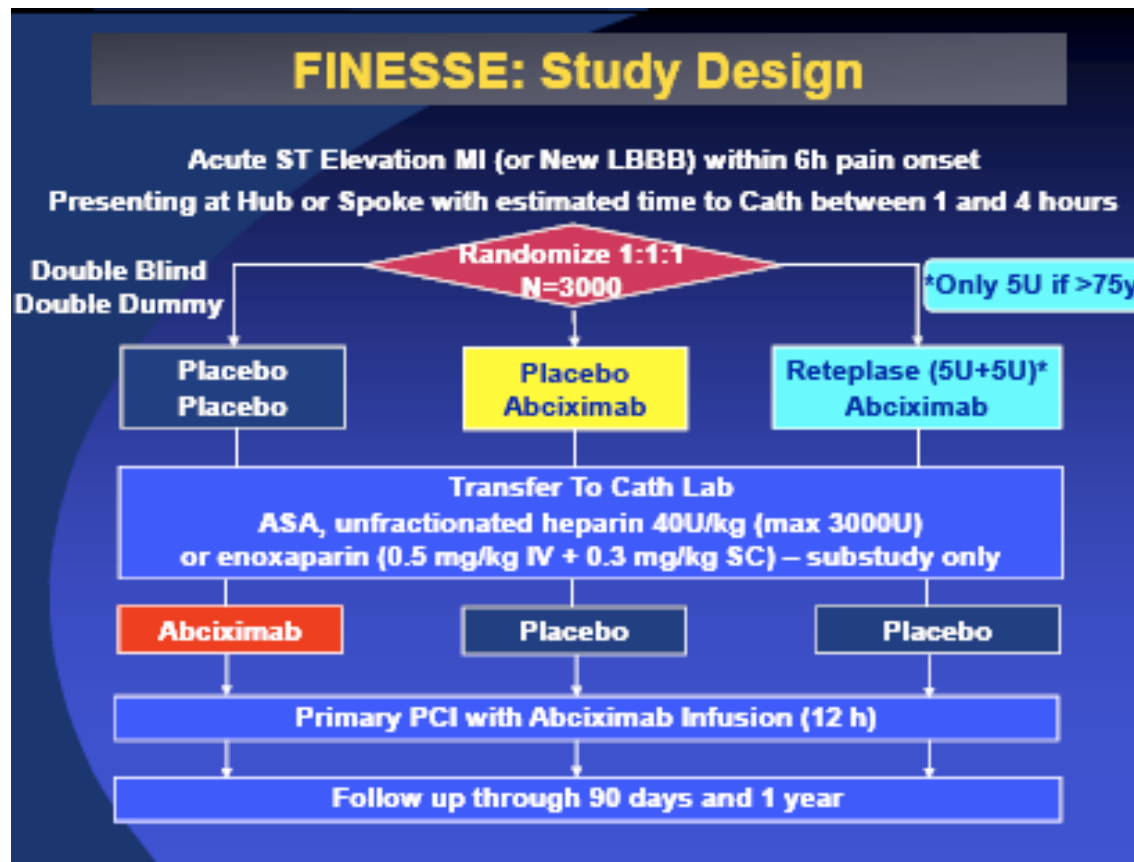
	Placebo n=477	Tirofiban n=473	p-value
Major	2.9%	4.00%	0.363
Minor	4.4%	6.1%	0.233
Non- CABG	2.7%	4.6%	0.807

Pas de variation TIMI, Blush, clinical endpoints saignements

Van't Hof et al.
Lancet 2008

SCA ST+

GPI: ± fibrinolytic
Abciximab ± half dose of
reteplase vs. placebo



Ellis et al. (16)
N Engl J Med 2008

SCA ST+

GPI ± fibrinolytic
 Abciximab ± half dose of
 reteplase vs. placebo

FINESSE Results: Primary and Secondary Endpoints

Endpoint	Primary PCI (%)	Abciximab-facilitated (%)	Combination (abciximab/ reteplase)-facilitated (%)	Combination -facilitated vs primary PCI (P)	Combination -facilitated vs abciximab-facilitated (P)
Primary endpoint*	10.7	10.5	9.8	NS	NS
All-cause mortality	4.5	5.5	5.2	NS	NS
Complications of MI	8.9	7.5	7.4	NS	NS
CHF requiring hospital/ ED visit	2.2	2.9	1.9	NS	NS
Death	4.5	5.5	5.2	NS	NS

* All cause mortality; rehospitalization or ED treatment for CHF; resuscitated ventricular fibrillation occurring > 48 hours after randomization; cardiogenic shock

ED=emergency department

Ellis S. European Society of Cardiology Congress 2007; September 3, 2007; Vienna, Austria

FINESSE Results: Safety (Bleeding) Endpoints

Endpoint	Primary PCI (%)	Abciximab-facilitated (%)	Combination (abciximab/ reteplase)-facilitated (%)	Combination-facilitated vs primary PCI (P)	Combination-facilitated vs abciximab-facilitated (P)
TIMI major bleeding	2.6	4.1	4.8	0.025	NS
TIMI minor bleeding	4.3	6.0	9.7	<0.001	0.006
TIMI major or minor bleeding	6.9	10.1	14.5	<0.001	0.008

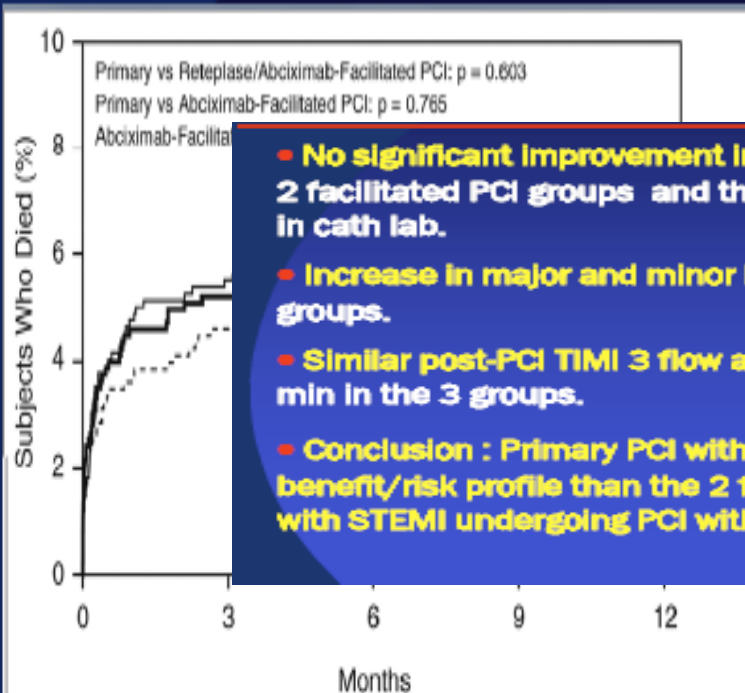
Ellis S. European Society of Cardiology Congress 2007; September 3, 2007; Vienna, Austria

Ellis et al. (16)
 N Engl J Med 2008

SCA ST+

GPI ± fibrinolytic
Abciximab ± half dose of
reteplase vs. placebo

FINESSE TRIAL RESULTS



- No significant improvement in primary endpoints between the 2 facilitated PCI groups and the group with PCI and abciximab in cath lab.
- Increase in major and minor bleeding in facilitated PCI groups.
- Similar post-PCI TIMI 3 flow and ST resolution at 180-240 min in the 3 groups.
- Conclusion : Primary PCI with in lab abciximab provides better benefit/risk profile than the 2 facilitated strategies in patients with STEMI undergoing PCI within 4 hrs of first medical contact.

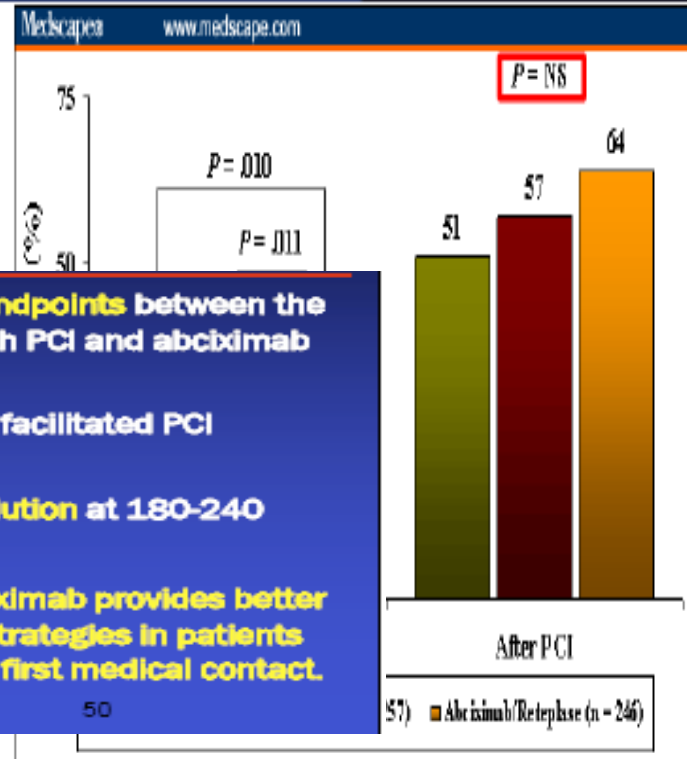
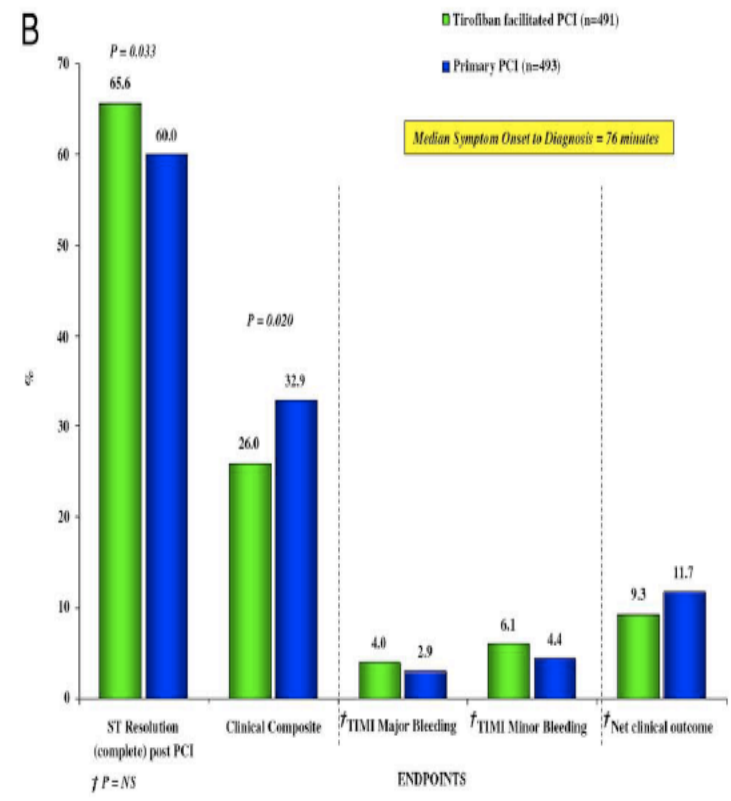
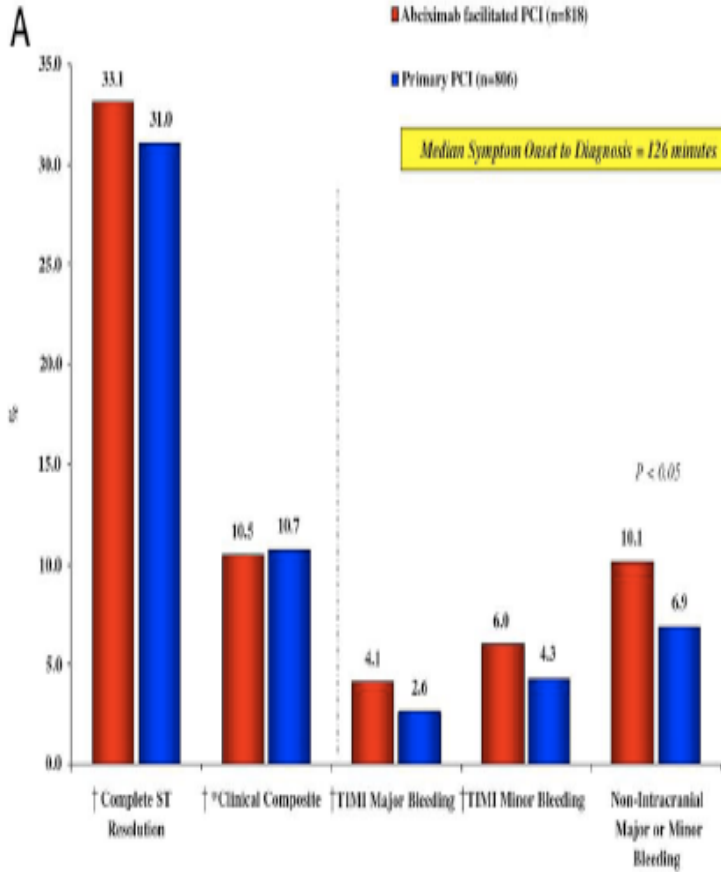


Figure 3.

FINESSE: ST-segment resolution before and after PCI.

Ellis et al. (16)
N Engl J Med 2008

FINESSE vs ON-TIME-2



Evolution thrombus % timing

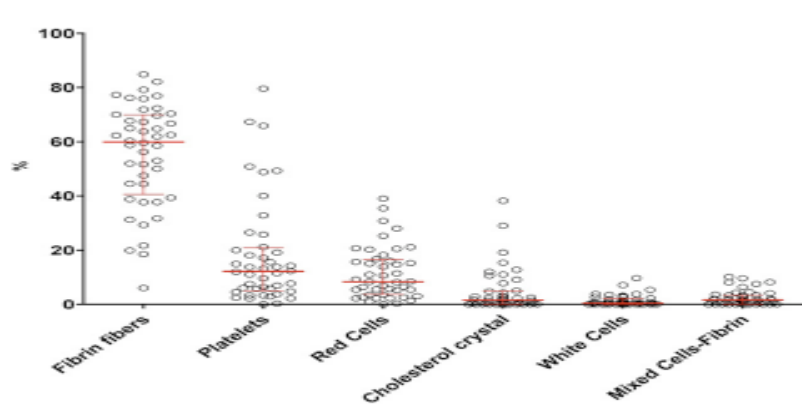


Figure 4 Thrombi Composition in 44 STEMI Patients (Early Presenters)

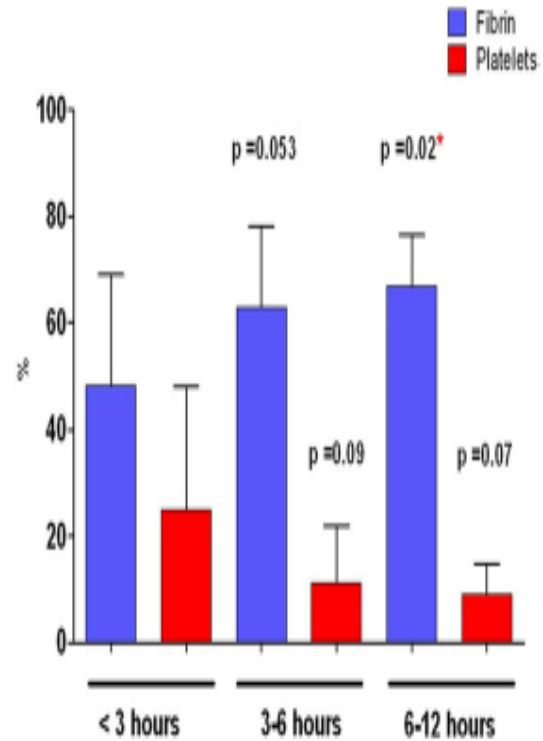


Figure 5 Impact of Time on Thrombus Composition

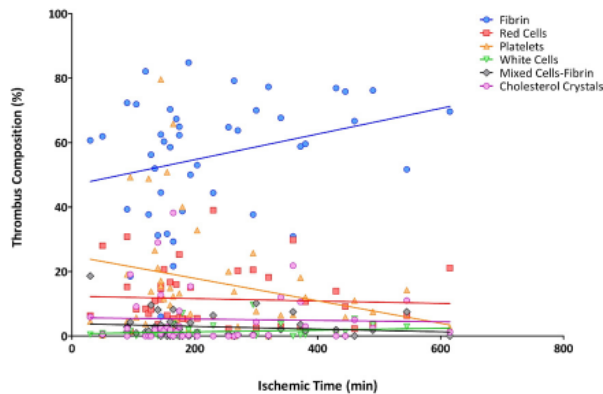


Figure 6 Evolution of the Percentage Thrombus Composition for Each Component

SCA ST+

DTI: bivalirudin vs. UFH
and GPI

HORIZONS AMI

3,602 pts with STEMI with symptom onset ≤ 12 hours

Aspirin, thienopyridine

R

1:1

UFH + GP IIb/IIIa inhibitor
(abciximab or eptifibatide)

Bivalirudin monotherapy
(\pm provisional GP IIb/IIIa)

Emergent angiography, followed by triage to primary PCI, CABG or medical therapy
3006 pts eligible for stent randomization

R

1:3

Paclitaxel-eluting TAXUS stent

Bare metal EXPRESS stent

Clinical FU at 30 days, 6 months,
1 year, and then yearly through 5 years

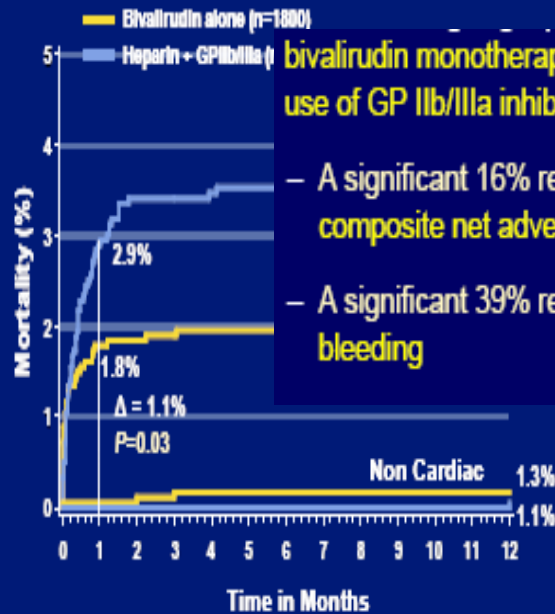
Stone GW. NEJM 2006;356:2218-30.

Stone et al. (78)
N Engl J Med 2008

SCA ST+

DTI: bivalirudin vs. UFH and GPI

1-Year Mortality: Cardiac and Non Cardiac



bivalirudin monotherapy compared to UFH plus the routine use of GP IIb/IIIa inhibitors resulted in:

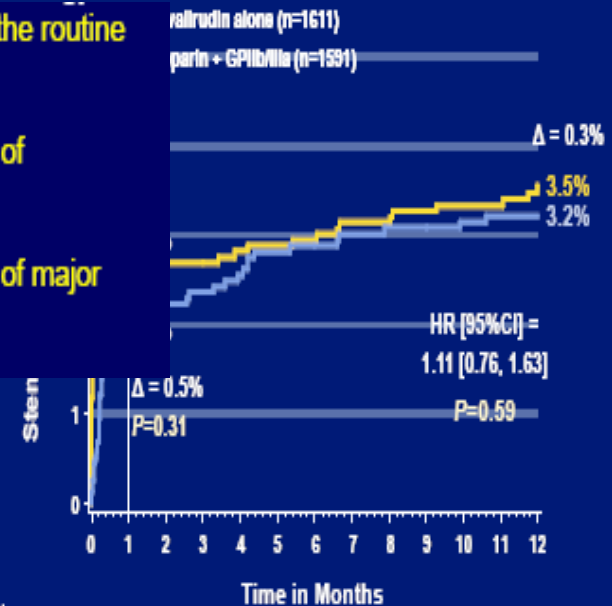
- A significant 16% reduction in the 1-year rate of composite net adverse clinical events
- A significant 39% reduction in the 1-year rate of major bleeding

Number at risk

	1800	1786	1684	1680	1520
Bivalirudin alone	1800	1786	1684	1680	1520
Heparin+GPIIb/IIIa	1882	1678	1683	1640	1488

Mehran R, TCT 2008

1-Year Stent Thrombosis (ARC Definite/Probable)



Number at risk

	1611	1626	1604	1488	1368
Bivalirudin alone	1611	1626	1604	1488	1368
Heparin+GPIIb/IIIa	1591	1486	1476	1467	1316

Mehran R, TCT 2008

Stone et al. (78)
N Engl J Med 2008

SCA ST + / quelle molecule?

- DANZI
- ERNST
- EVA AMI
- FATA
- MULTISTRATEGY
- STRATEGY
- SCAAR

SCA ST + / quelle molecule ?

J Am Coll Cardiol. 2009; 53:1668-1673, doi:10.1016/j.jacc.2009.01.053
 © 2009 by the American College of Cardiology Foundation

CLINICAL RESEARCH: INTERVENTIONAL CARDIOLOGY

Benefits From Small Molecule Administration as Compared to Abciximab Among ST-Segment Elevation Myocardial Infarction Treated With Primary Percutaneous Coronary Intervention

A Meta-Analysis

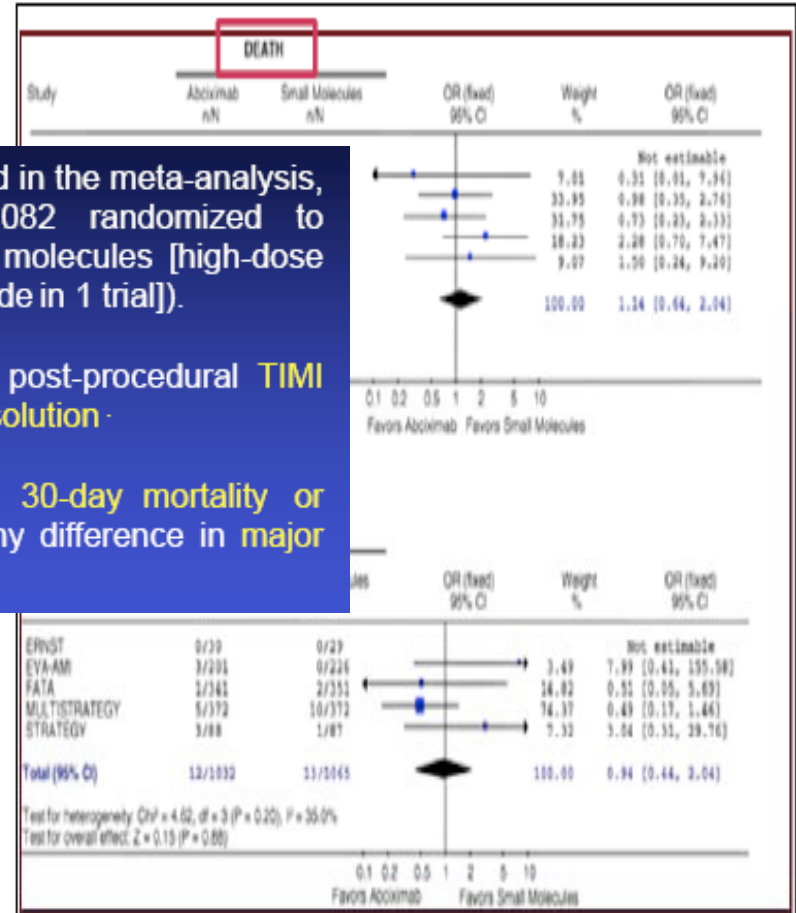
Giuseppe De Luca, MD*, Grazia Ucci, MD,
 Ettore Casetti, MD and Paolo Marino, MD

➤ A total of **6 RTs** were included in the meta-analysis, involving **2,197** patients (1,082 randomized to abciximab and 1,115 to small molecules [high-dose tirofiban in 5 trials and eptifibatide in 1 trial]).

Compared to small molecules:

➤ Abciximab did not improve post-procedural **TIMI flow grade 3 or ST-segment resolution**.

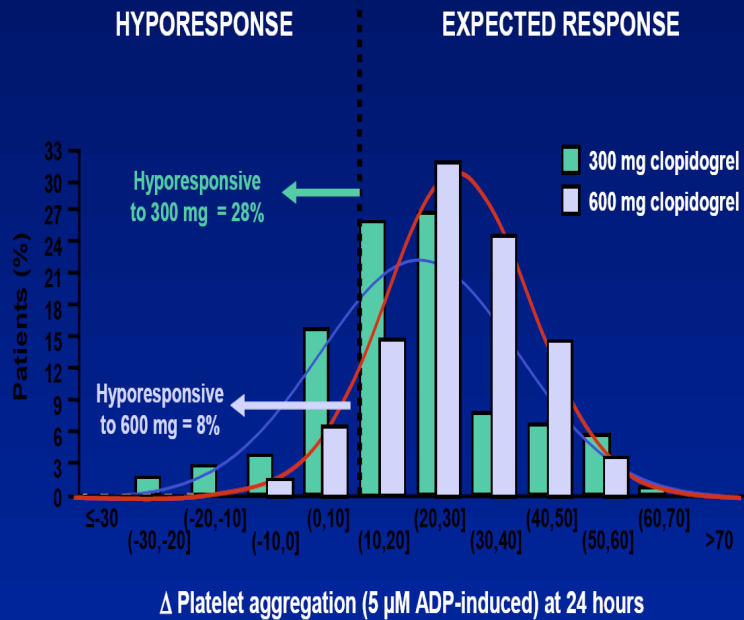
➤ Abciximab did not reduce **30-day mortality or reinfarction**, nor was there any difference in **major bleeding complications**.



Place des PGI % nouveaux AAP

Clopidogrel Response Variability: 300 mg vs 600 mg

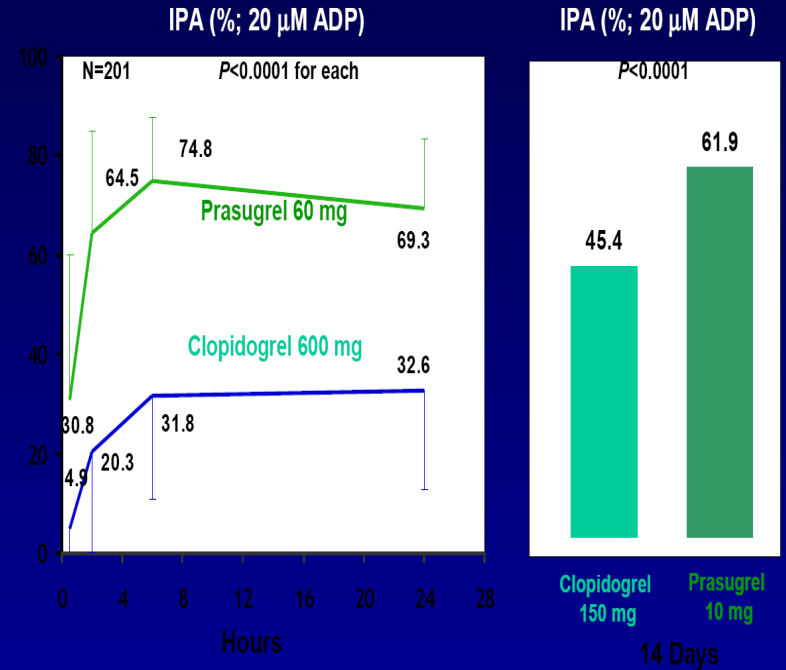
N=190



Gurbel PA, et al. *J Am Coll Cardiol.* 2005;45(9):1392-1396.

PRINCIPLE TIMI 44:

Prasugrel vs Higher Dose Clopidogrel



PRINCIPLE TIMI 44 = The Prasugrel in Comparison to Clopidogrel for Inhibition of Platelet Activation and Aggregation-Thrombolysis in Myocardial Infarction 44.
Wiviott SD, et al. *Circulation.* 2007;116(25):2923-2932.

ticagrelor



UA/NSTEMI (mod-high risk)
STEMI (if primary PCI)
All Receiving ASA
Clopidogrel Treated or Naïve

n=18,000 pts

Clopidogrel
If pretreated, no additional load;
if naïve, standard 300 mg load,
then 75 mg od maintenance
(additional 300 mg allowed pre-PCI)

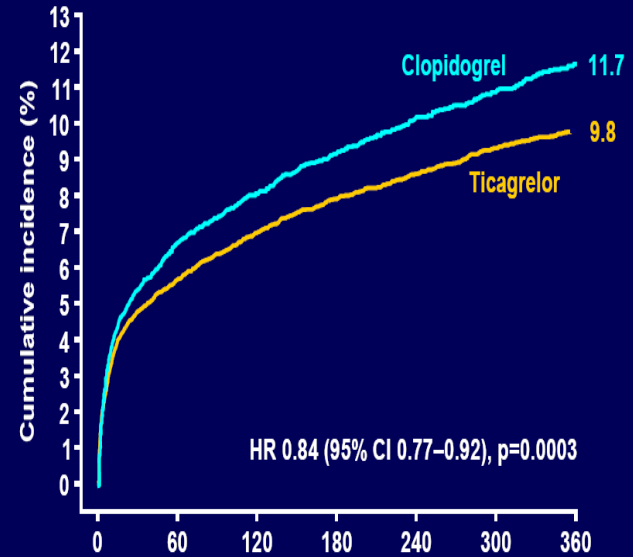
AZD6140
180 mg load, then
90 mg bid maintenance
(additional 90 mg pre-PCI)

12 month maximum exposure
(Min=6 mo, max=12 mo, mean=11 mo)

Primary Endpoint: CV Death/MI/Stroke
**Secondary EP: CV Death/MI/Stroke/Revascularization with PCI;
CV Death/MI/Stroke; Severe Recurrent Ischemia**

ClinicalTrials.gov Identifier: NCT00391872

K-M estimate of time to first primary efficacy event (composite of CV death, MI or stroke)



	Days after randomisation						
No. at risk	0	60	120	180	240	300	360
Ticagrelor	9,333	8,628	8,460	8,219	6,743	5,161	4,147
Clopidogrel	9,291	8,521	8,362	8,124	6,743	5,096	4,047

prasugrel



STUDY DESIGN

ACS (STEMI or UA/NSTEMI) & Planned PCI

ASA ↓ N = 13,000

Double-blind

CLOPIDOGREL

300 mg LD/ 75 mg MD

60 mg LD/ 10 mg MD

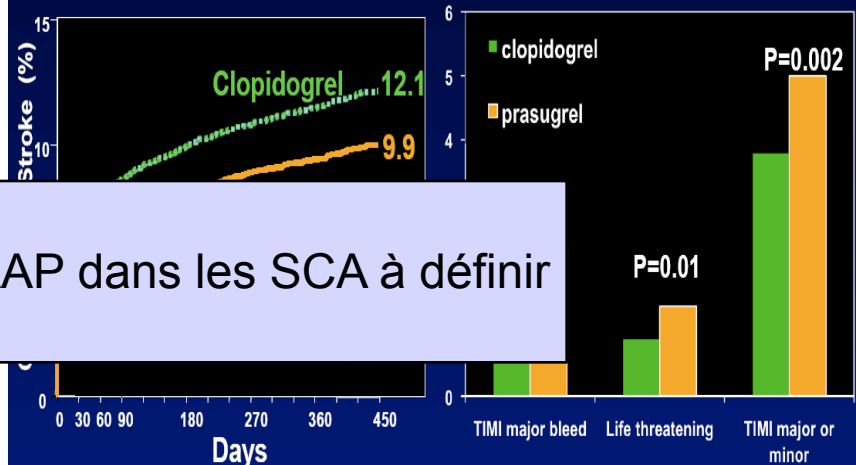
Median duration of therapy - 12 months

1° endpoint: CV death, MI, Stroke
2° endpoints: CV death, MI, Stroke, Rehosp-Rec Isch
CV death, MI, UTVR

Wiviott et al, AHJ 2006

TRITON TIMI-38 STEMI cohort

TRITON-TIMI 38



Wiviott et al. *New Engl J Med* 2007;357:2001-2015

TRITON allowed recruitment of STEMI patients undergoing primary PCI when they presented < 12 hours of symptom onset or secondary PCI when they presented late

Evaluer le risque ischémique /hémorragique adapter la stratégie

GRACE Risk Score

Variable	Odds ratio
Older age	1.7 per 10 y
Killip class	2.0 per class
Systolic BP	1.4 per 20 mm Hg ↑
ST-segment deviation	2.4
Cardiac arrest during presentation	4.3
Serum creatinine level	1.2 per 1-mg/dl ↑
Positive initial cardiac biomarkers	1.6
Heart rate	1.3 per 30-beat/min ↑

The sum of scores is applied to a reference nomogram to determine the corresponding all-cause mortality from hospital discharge to 6 months. Eagle KA, et al. JAMA 2004;291:2727-33. The GRACE clinical application tool can be found at www.outcomes-umassmed.org/grace. Also see Figure 4 in Anderson JL, et al. J Am Coll Cardiol 2007;50:e1-e157. GRACE = Global Registry of Acute Coronary Events.

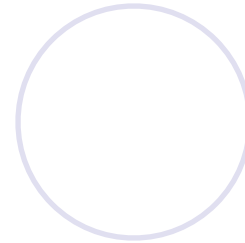
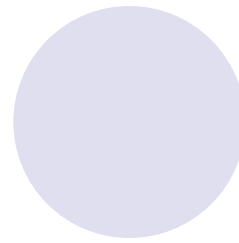
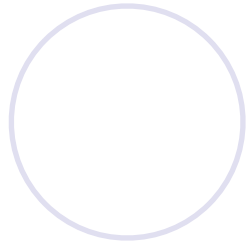
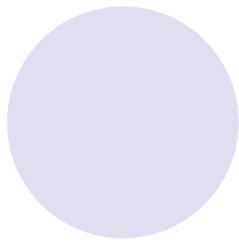
En conclusion : place des GPI en 2011

● **SCA non ST+**

- Pas intérêt upstream systématique (eptifibatide)
- Risque > saignement (EARLY ACS)
- A utiliser si haut risque ischémique (+/- ST change tropo+, diabète, GRACE score+)
- En cas de coro programmée
- % lésions angio, avant PCI
- Intérêt GPI downstream + dose charge AAP (600 mg clopidogrel ISAR react)

● **SCA ST+**

- Abciximab molécule la + étudiée
- Résultats controversés en upstream
- résolution ST /on time (+)
- Taille IDM(=), mortalité (=)/Brave 3
- Abciximab in lab > facilitée /combinée
- Intérêt usage précoce, haut risque ischémique, bas risque hémorragique
- VOIE RADIALE



● Merci de votre attention !

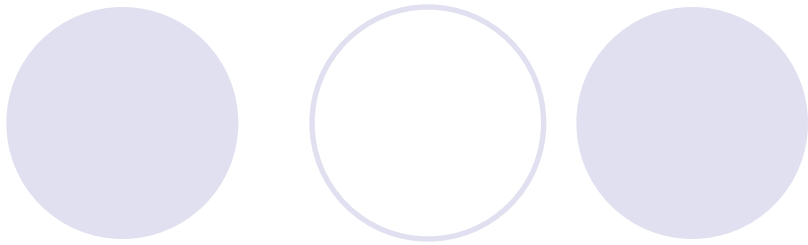




CONCLUSION

• ST ELEVATION ACS:

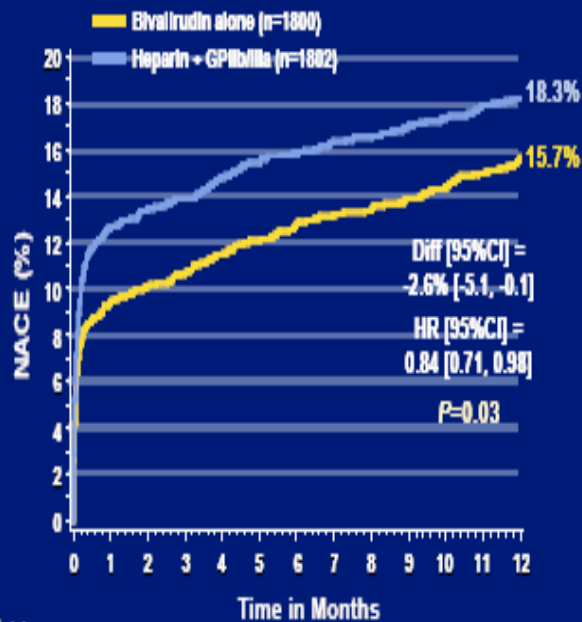
- Most studies of GPIIb-IIIa inhibitors in STEMI have evaluated abciximab (0.25 mg/kg i.v. bolus followed by infusion of 0.125 mg/ kg/min up to a maximum of 10 mg/min for 12 h).
- Findings are mixed regarding the effectiveness of facilitation (early administration) with GPIIb-IIIa inhibitors before catheterization. While several RCTs showed no benefit, registries, meta-analyses, and post hoc analyses of APEX-AMI show positive results.
- The controversial literature data, the negative outcome of RCTs, and the beneficial effects of faster acting and more efficacious ADP receptor blockers in primary PCI **do not support pre-hospital or pre-catheterization use of GPIIb-IIIa inhibitors.**

- 
- SCA ST+
 - Abciximab molécule la + étudiée
 - Resultats controversés en upstream
 - resolution ST /on time (+)
 - Taille IDM(=), mortalité (=)/Brave 3
 - Abciximab in lab > facilitée
 - Interet usage precoce , haut risque ischémique , bas risque hémorragique

SCA ST+

DTI: bivalirudin vs. UFH and GPI

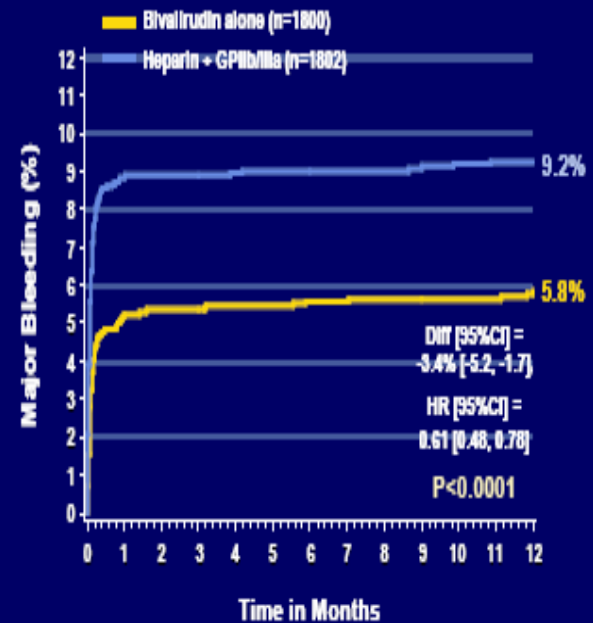
1-Year Net Adverse Clinical Events*



*NACE or major bleeding (non CABG)

Mehran R, TCT 2008

1-Year Major Bleeding (non-CABG)



Mehran R, TCT 2008

Stone et al. (78)
N Engl J Med 2008