

Tct Asia Pacific

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Pharmaco-invasive strategies for acute myocardial infarction: the CARESS-in-AMI Trial

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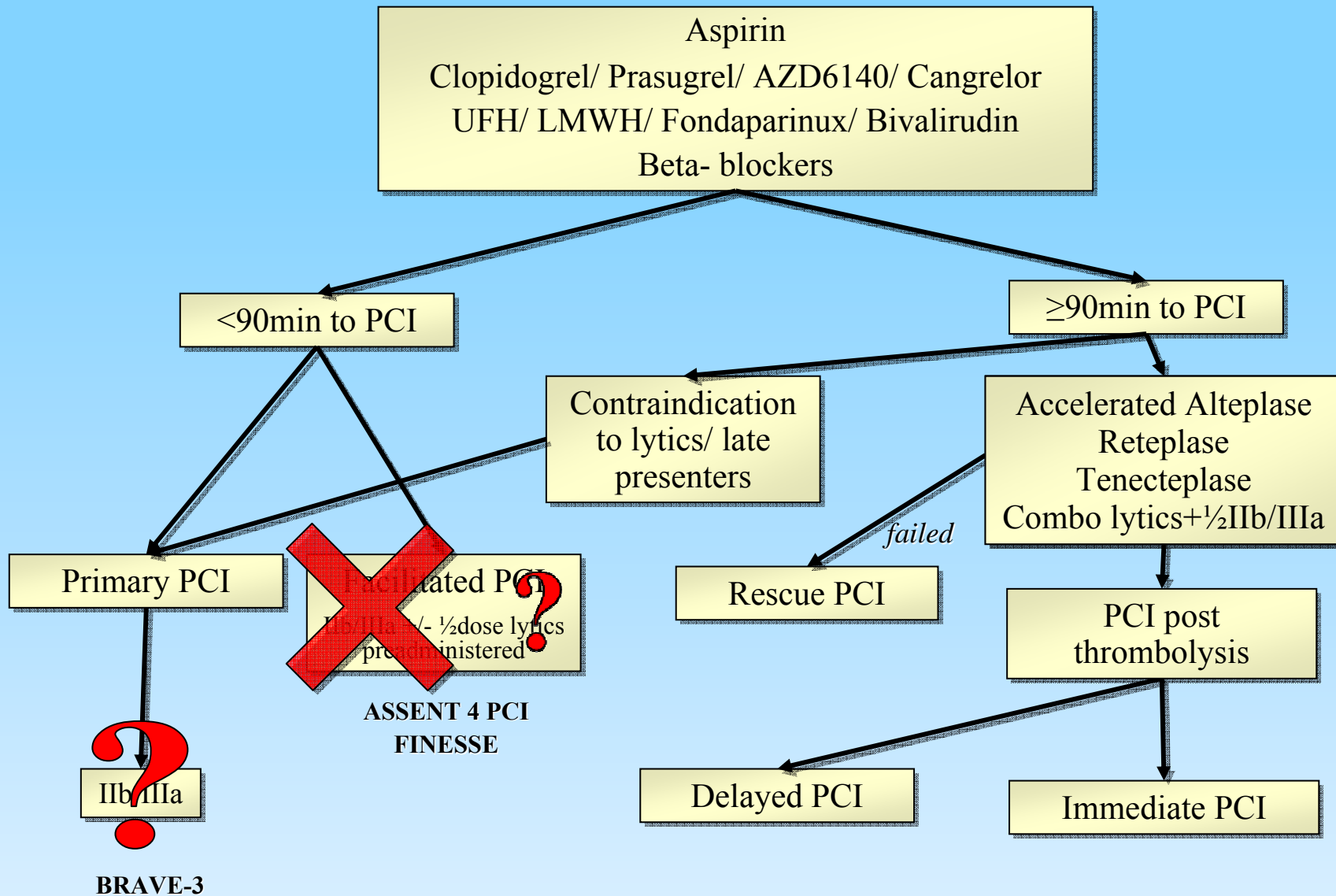
President Elect EAPCI-ESC



**Imperial College
London**

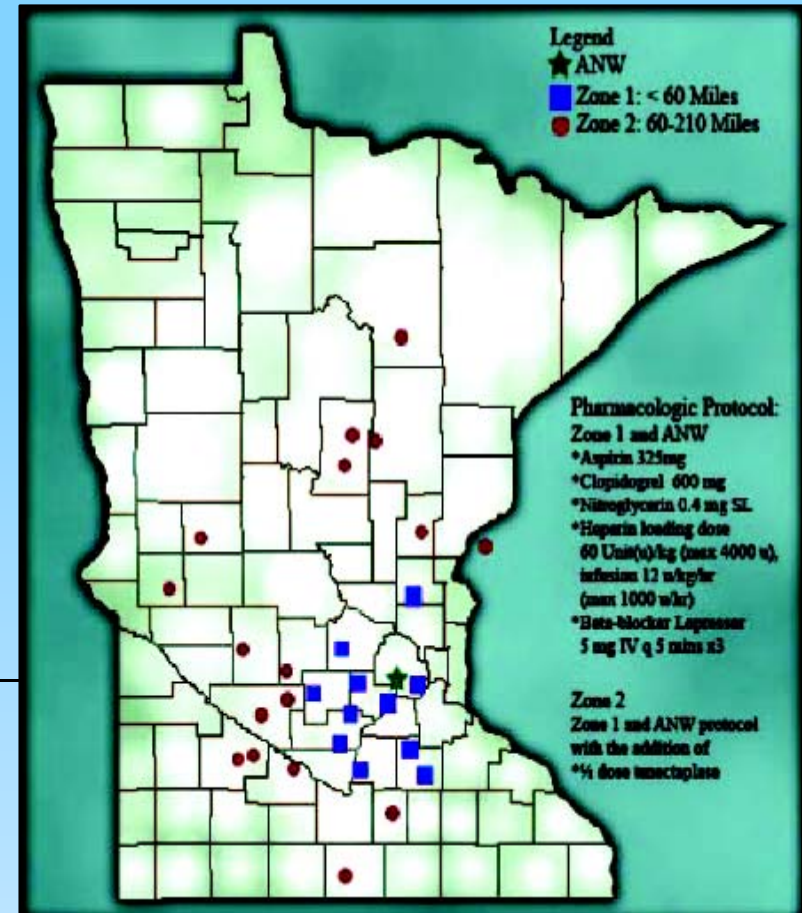
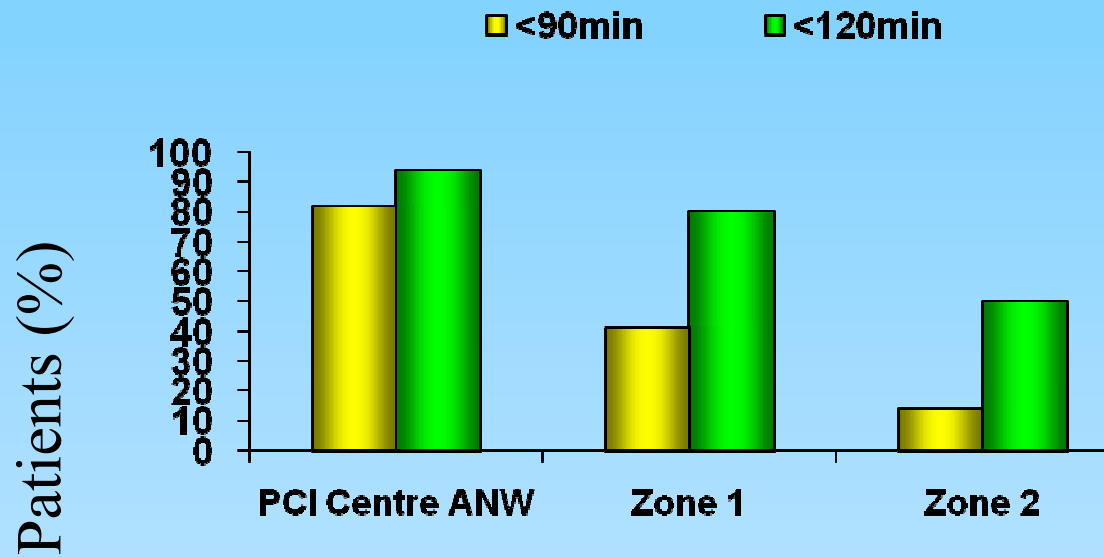
PHARMACOINVASIVE STRATEGIES IN ACUTE MI

STEMI





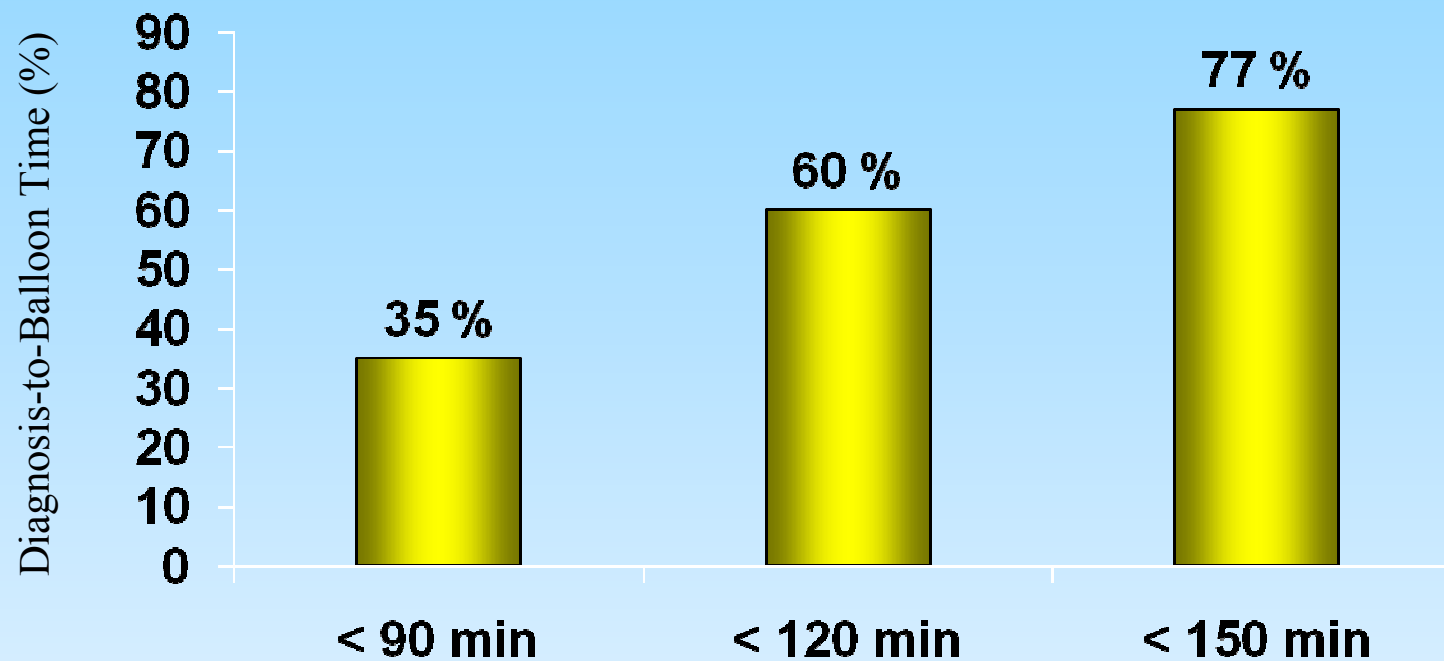
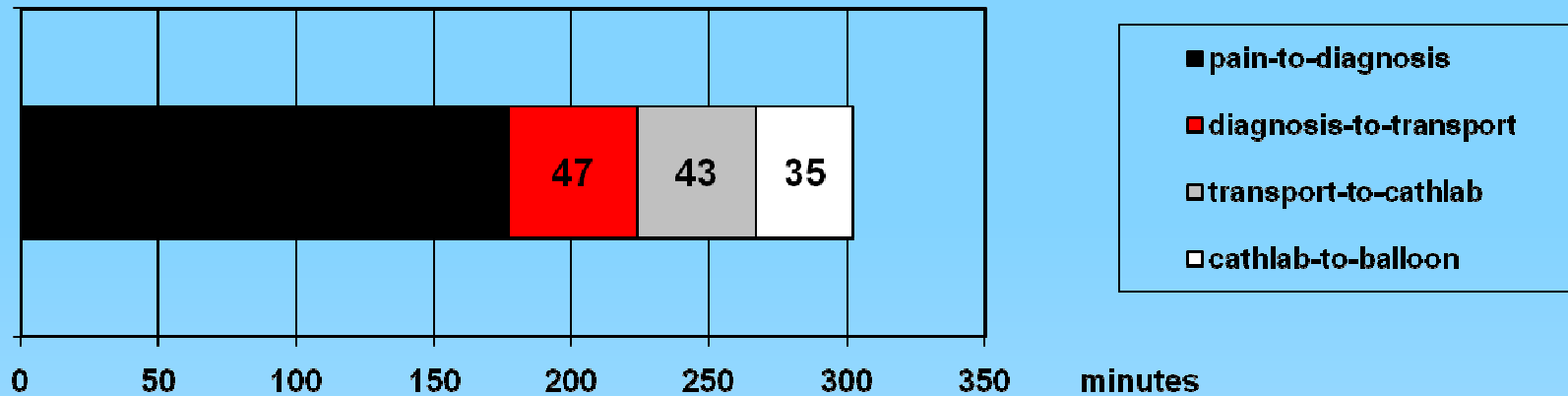
1,345 Pts Consecutively Treated in the Regional PCI System for STEMI Minneapolis-Minnesota Network between 2003 and 2006



n=297 <60 miles 60-120 miles
 n=627 n=421

73% Pts Transported
by Helicopter

1,650 consecutive STEMI pts in the EUROTRANSFER Registry ; 7 european countries from 2005 to 2007



Dudek, Siudak, Janzon et al. ESC 2007



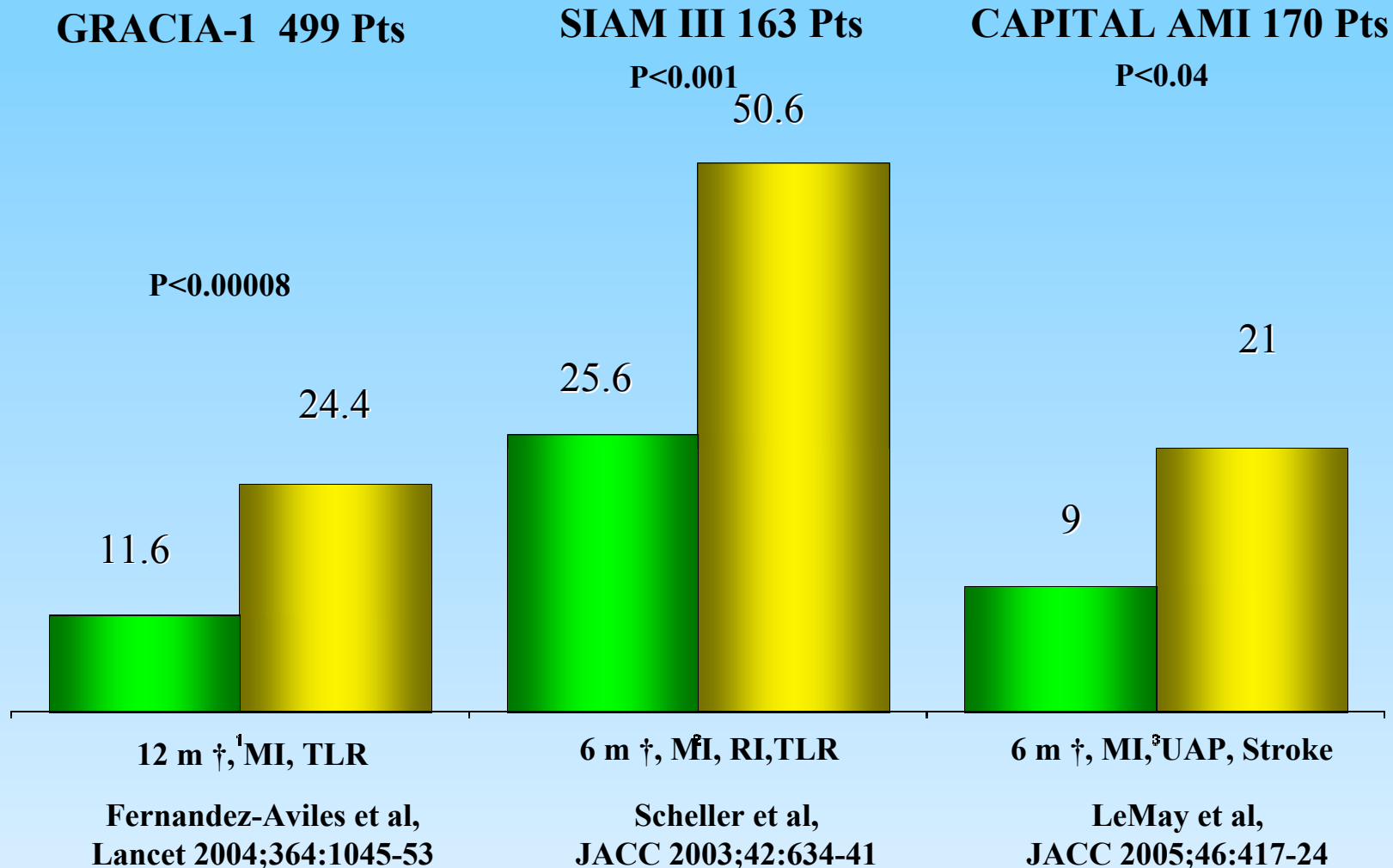
Immediate (within 24h) or Deferred PCI after Lysis



Lytics + angio within 24 hrs

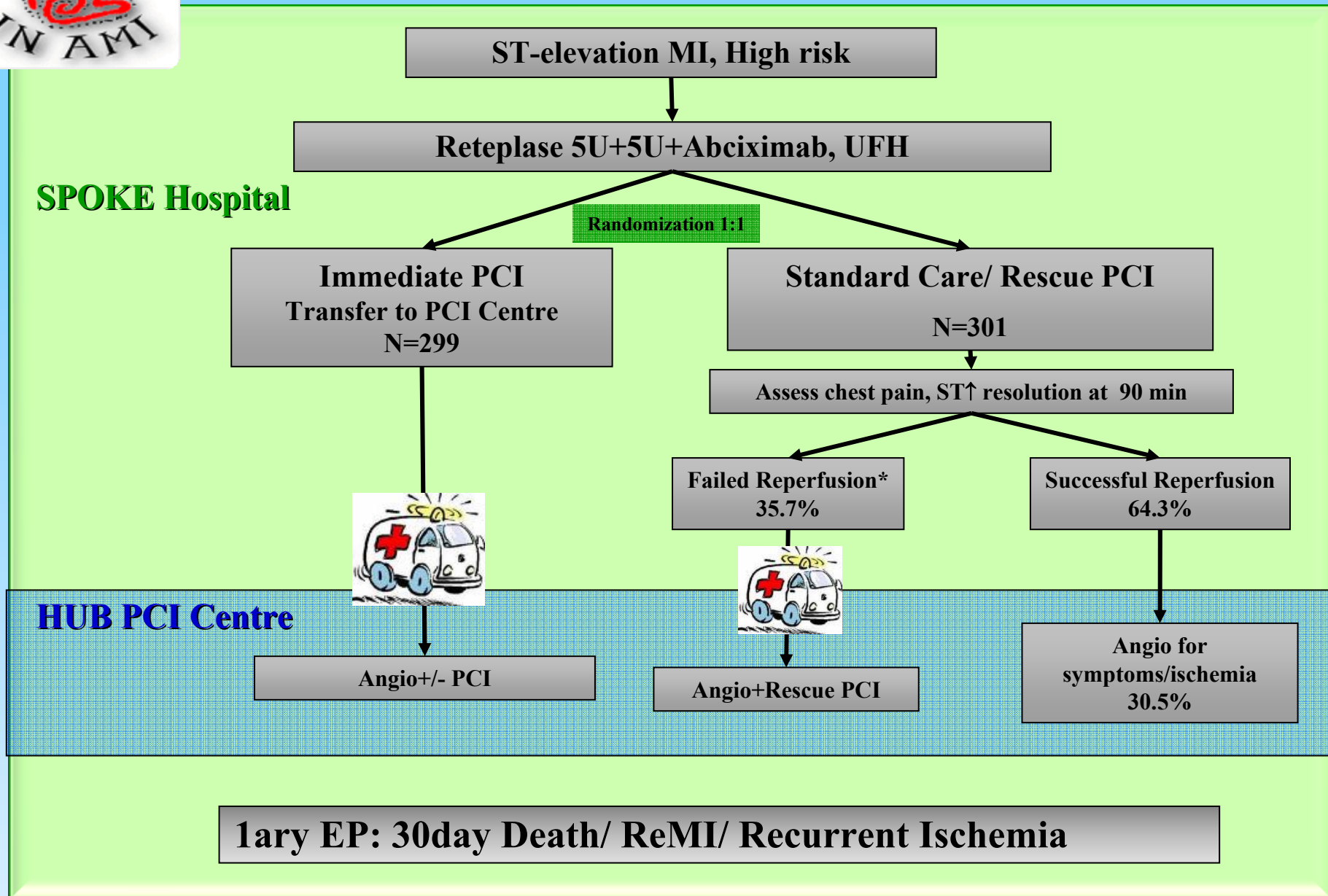


Lytics + angio when clinically mandated





PHARMACONVASIVE STRATEGIES IN ACUTE MI

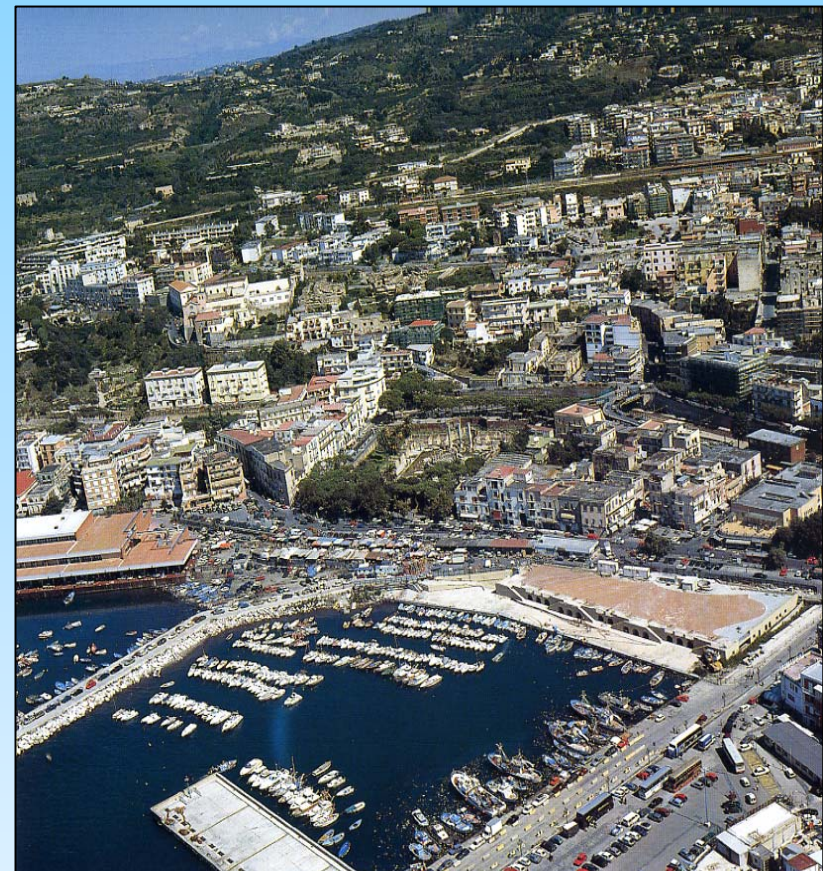
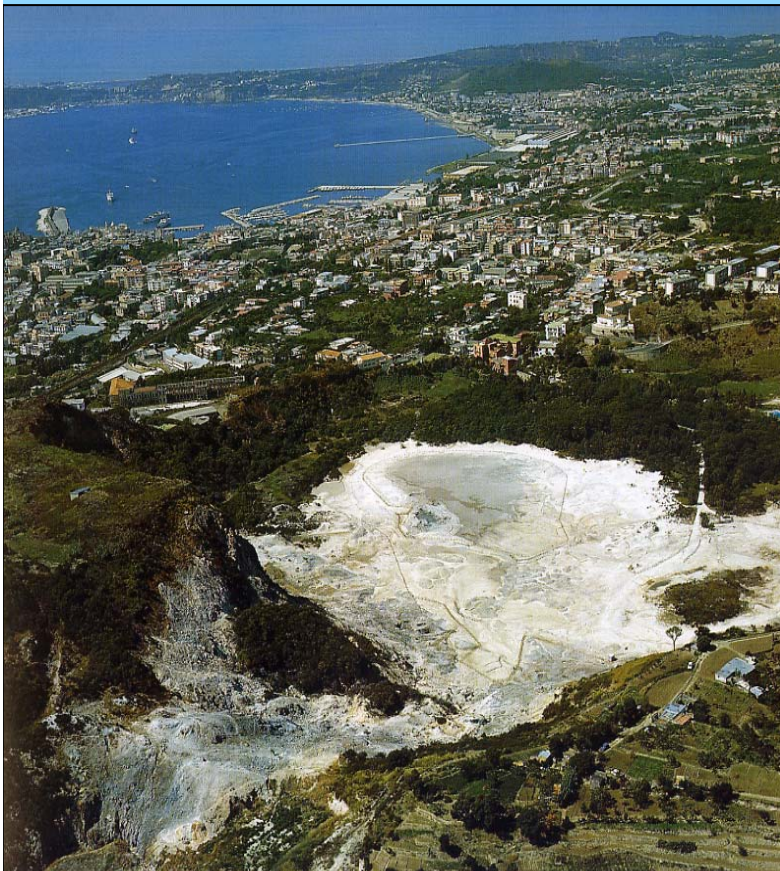


Di Mario et al. Lancet 2008;371:559-68



Pozzuoli, 22 November 2006, 14:33

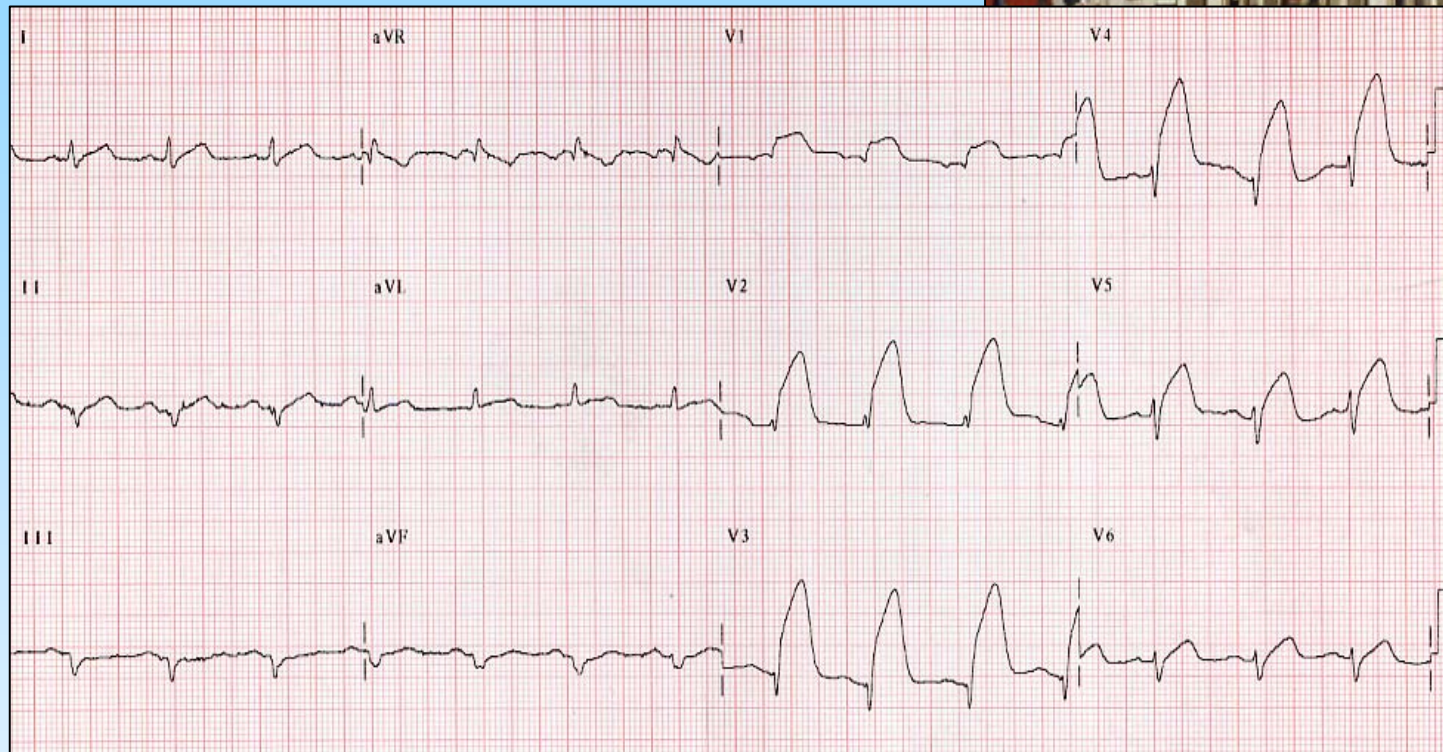
- 60 Yr old man, type II DM treated with oral antidiabetic drugs; Heavy smoker (40 cigarettes); Hypertension; Dyslipidaemia; ECG evidence of previous (silent) inferior MI





Pozzuoli 22 November 2006: 16:34, Bolus given

- Aspirin 150 mg + Clopidogrel 300
- Reteplase 5 U
- Heparin 40 mg/Kg
- Abciximab 25 μ g/Kg





On the Road: 55 min transfer time, arrival 17:58

Reteplase 5 U 2nd bolus after 30 m'
Heparin 7 U/Kg/hour
Abciximab 0.125 mcg/Kg/min
Chest pain disappears





18:11 First Angio Naples

Before PTCA: TIMI 3

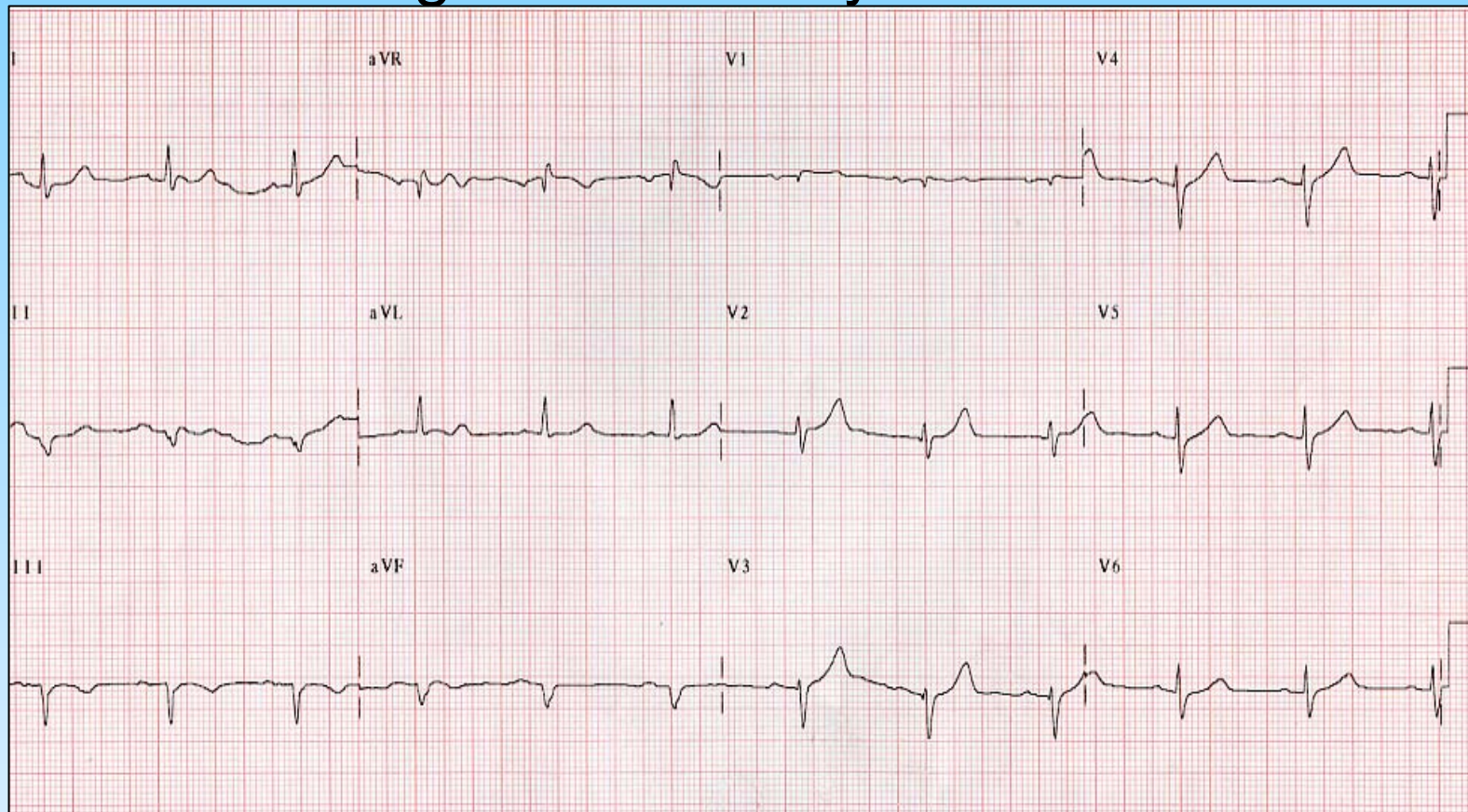
AFTER Taxus





ECG 90 minutes after PCI

- AngioSeal 6 Fr: no haematoma
- Uneventful hospital stay
- Discharged after 4 days

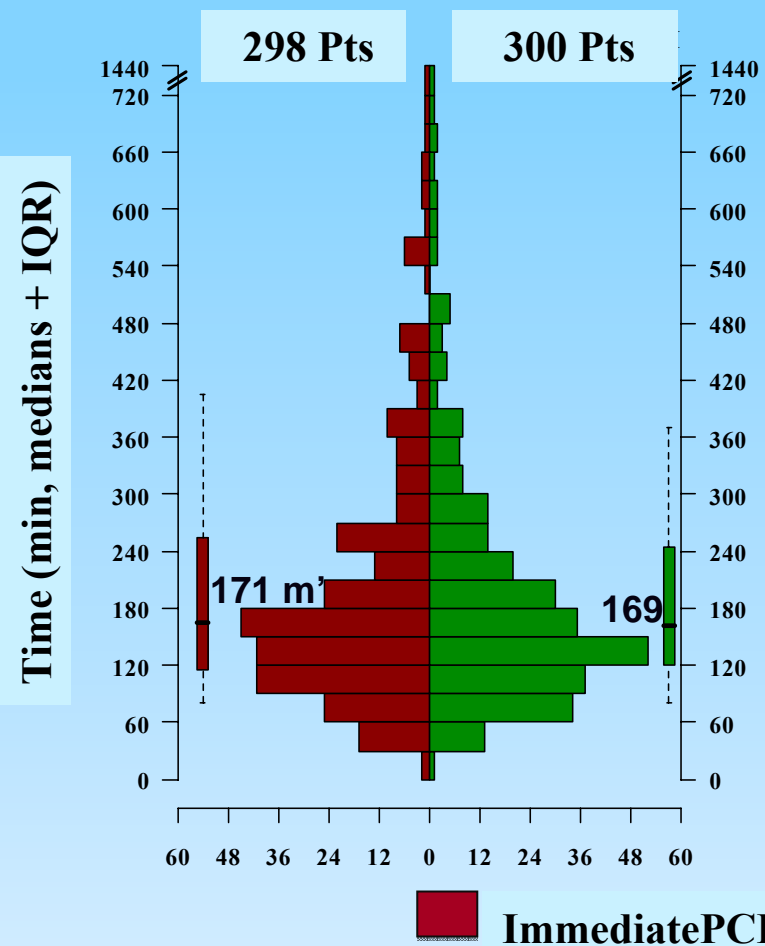




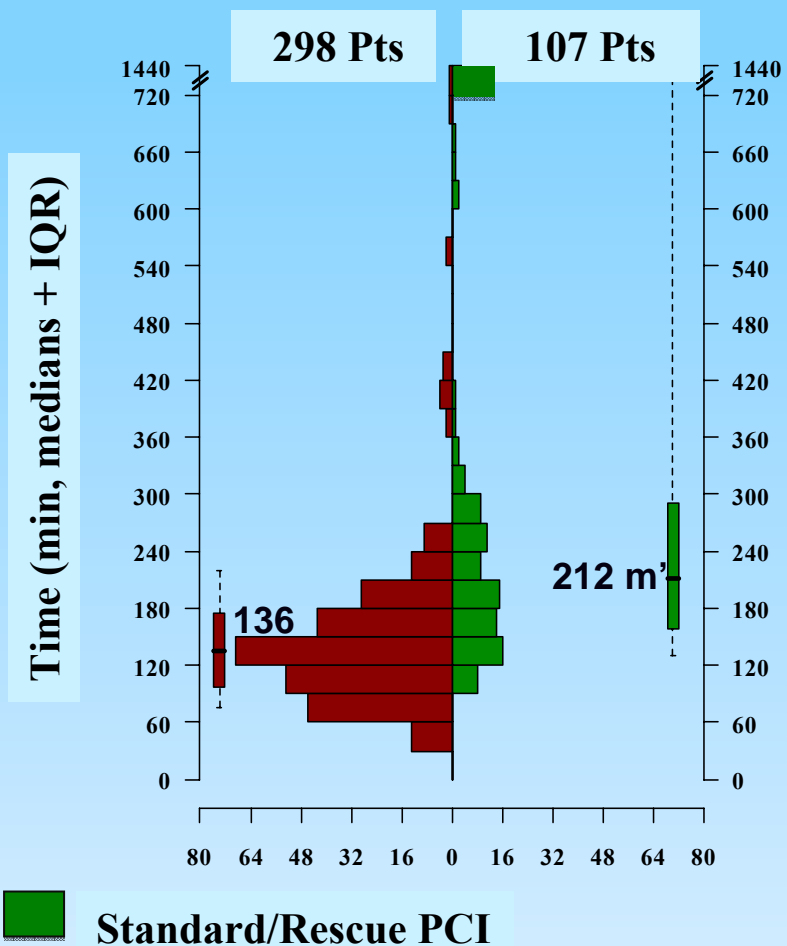
PHARMACOINVASIVE STRATEGIES IN ACUTE MI

CARESS-in-AMI

Symptom Onset to Reteplase

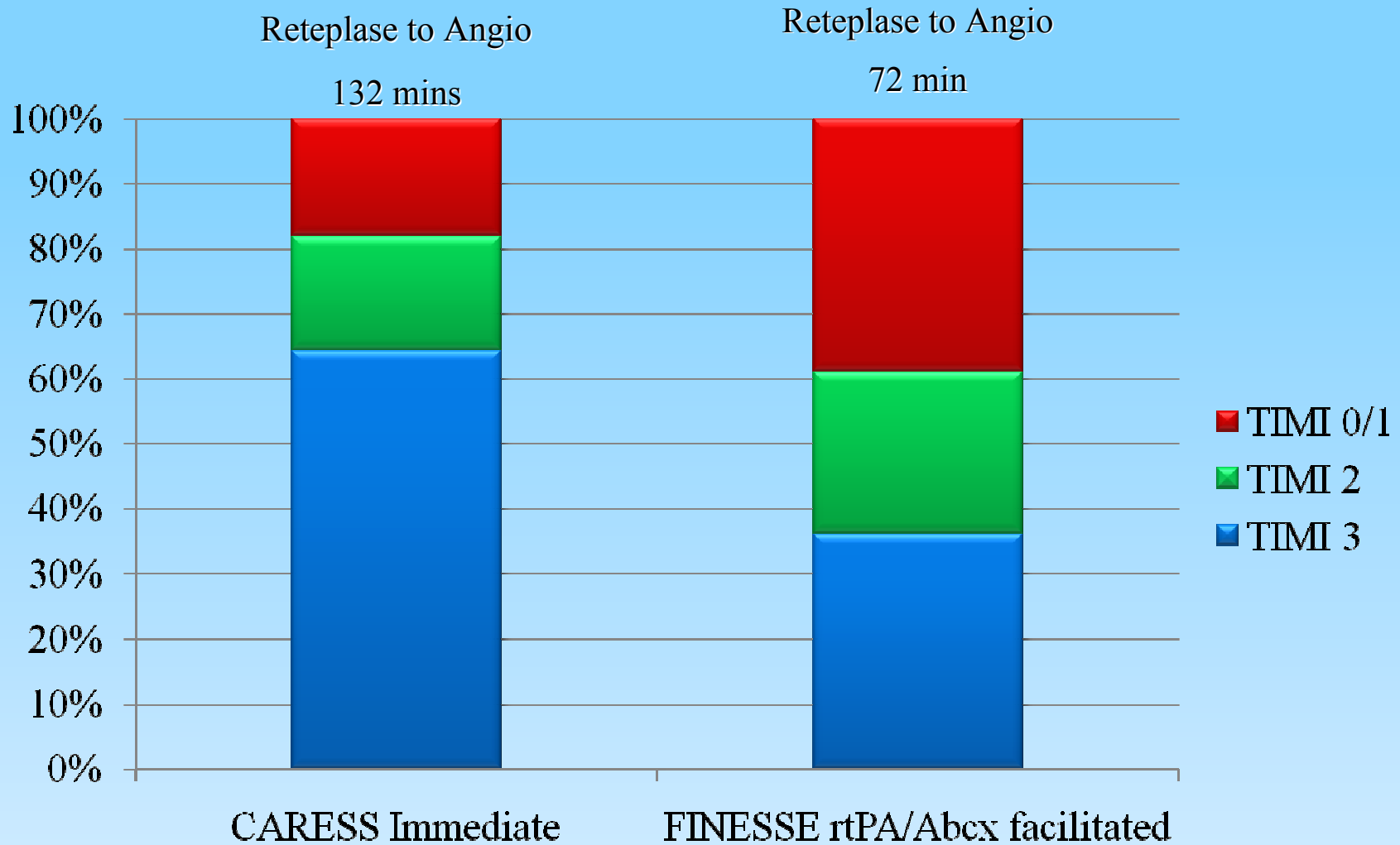


Reteplase to Angiography



Di Mario et al. Lancet 2008;371:559-68

TIMI flow pre in CARESS and FINESSE



Di Mario et al. Lancet 2008;371:559-68

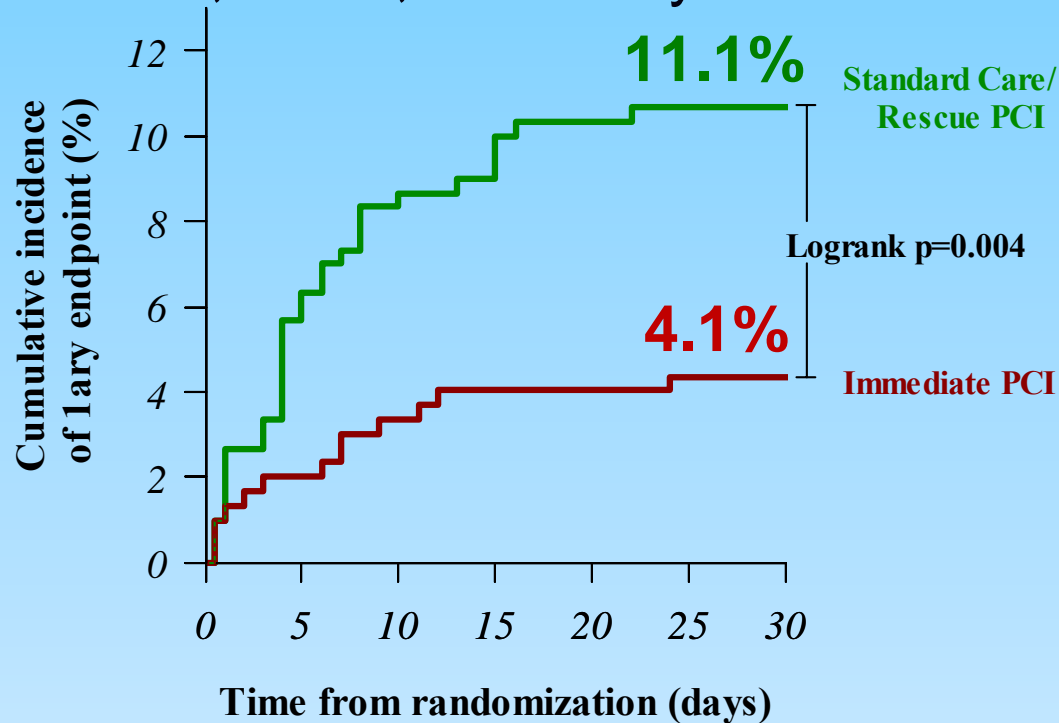
Ellis et al. NEJM 2008 in press



PHARMACOINVASIVE STRATEGIES IN ACUTE MI

CARESS-in-AMI

Primary Endpoint
Death, re-MI, refractory ischaemia



OR 0.34

(95%CI 0.17-0.68)

P=0.001

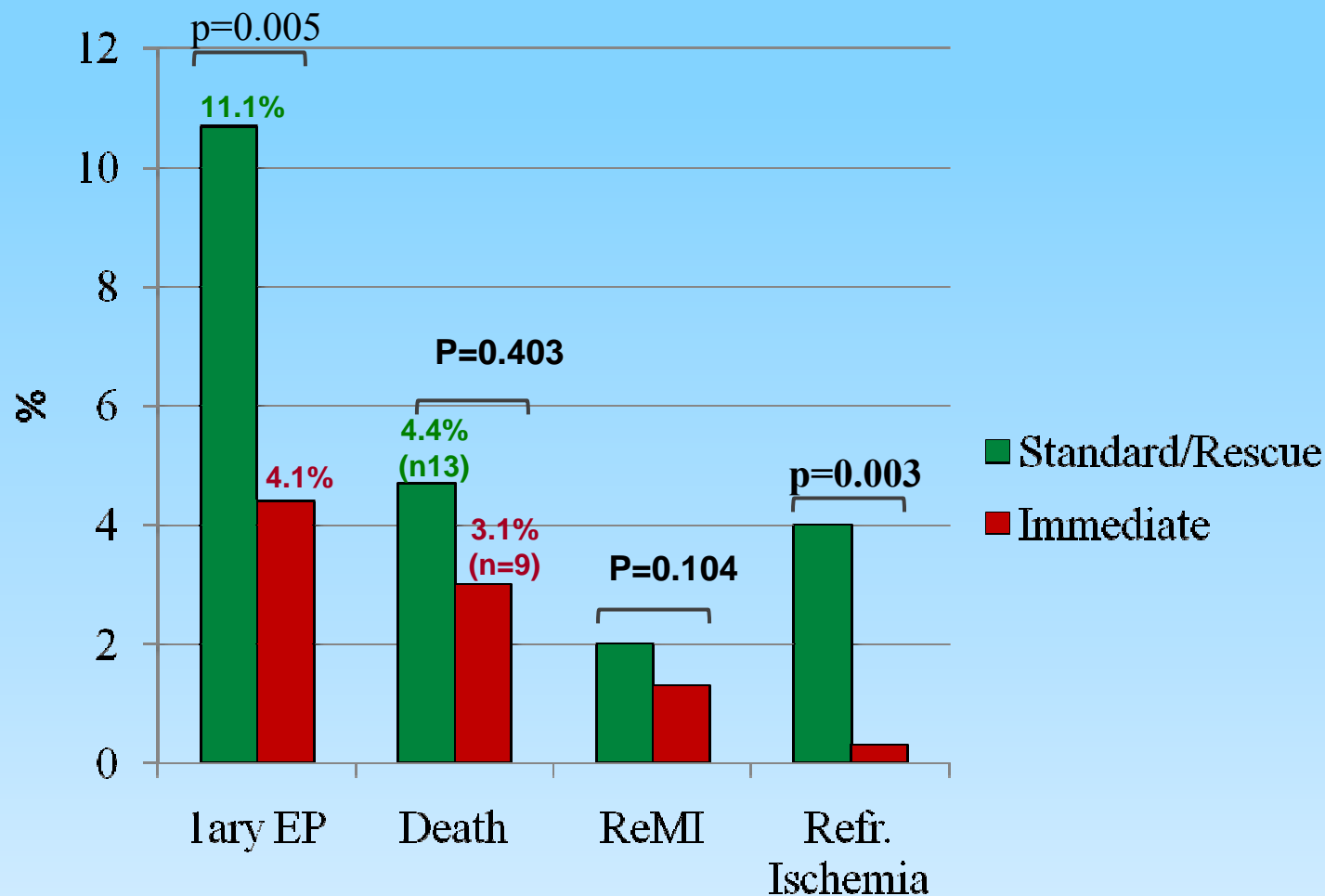
<i>Standard/Rescue</i>	300	283	275	273	269	268	268
<i>Immediate PCI</i>	298	292	287	285	285	284	284

Di Mario et al. Lancet 2008;371:559-68



PHARMACOINVASIVE STRATEGIES IN ACUTE MI

CARESS-in-AMI

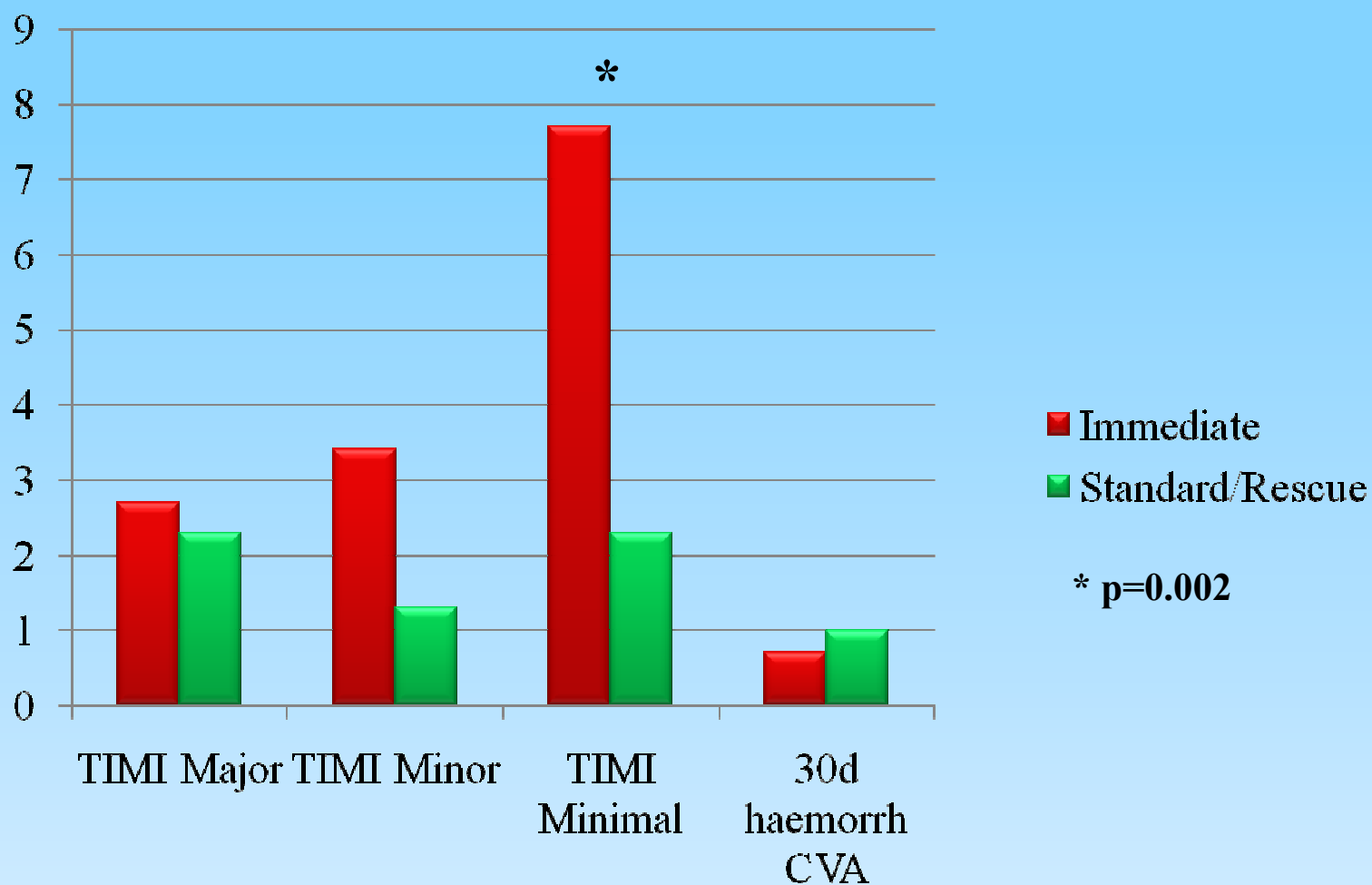


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PHARMACOINVASIVE STRATEGIES IN ACUTE MI

CARESS-in-AMI



Di Mario et al. Lancet 2008;371:559-68

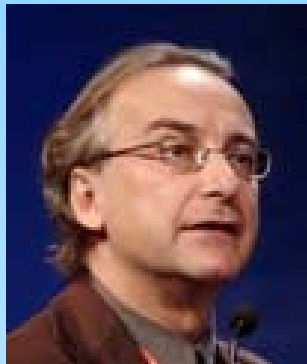


Criticisms & Comments

F. Verheugt, commentator ESC 2007



- ❖ Neither clopidogrel nor LMWH were used
- ❖ Early PCI after lytics is clearly beneficial but when: 17 hours as in GRACIA-1 or immediate?



N. Danchin, Editorial Comment, Lancet 2008;

- ❖ The trial suggests a benefit but it was stopped before scheduled recruitment was completed and numbers are too low to confirm it

Owen, Letter, Lancet 2008, in press

- ❖ Combo therapy with 2b-3a inhibitors is not a recommended lytic regimen in Guidelines. An approved lytic type and dose should be tested

Clopidogrel trials in comparison

CLARITY

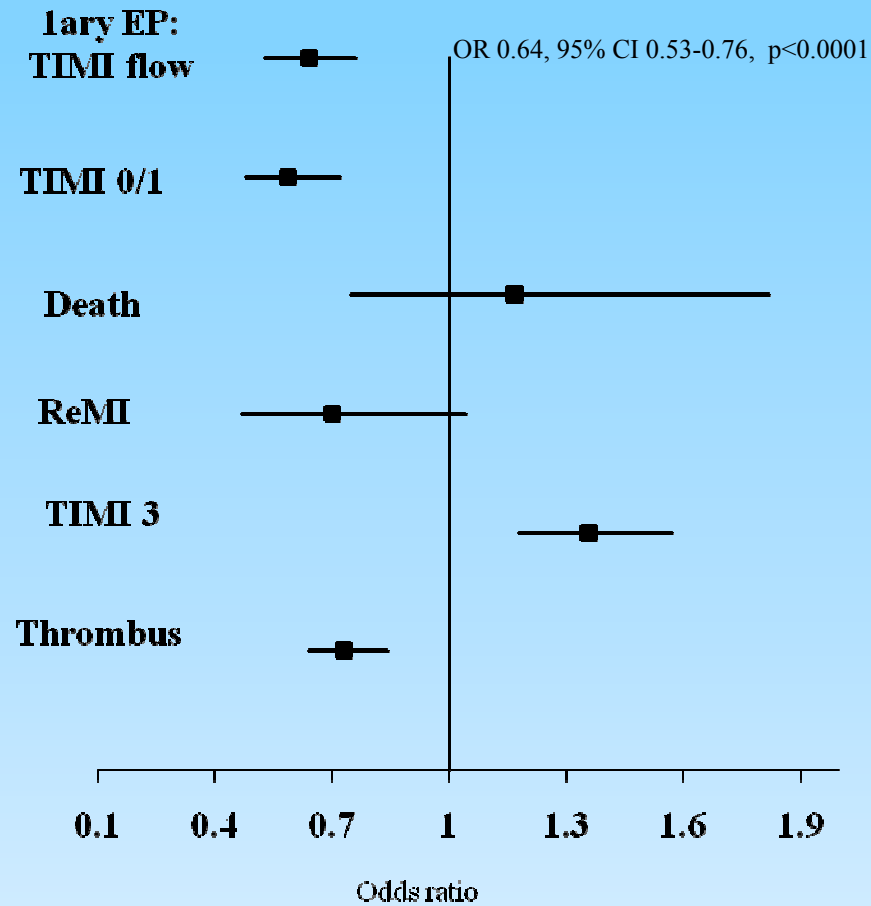
- 1ary EP: TIMI flow on angio
- n=3500
- MI < 12 hrs
- ≤ 75 years
- 100% Fibrinolytic
- Loading dose 300mg
- Angio 2-8 days
- Europe / North America

COMMIT/ CCS-2

- 1ary EP: Mortality, Death/MI/CVA
- n=46000!
- MI < 24 hrs
- ≤ 100 years!
- ~50% Fibrinolytic (also SK)
- No loading dose
- Non-invasive Strategy
- China

CLARITY

n=3500

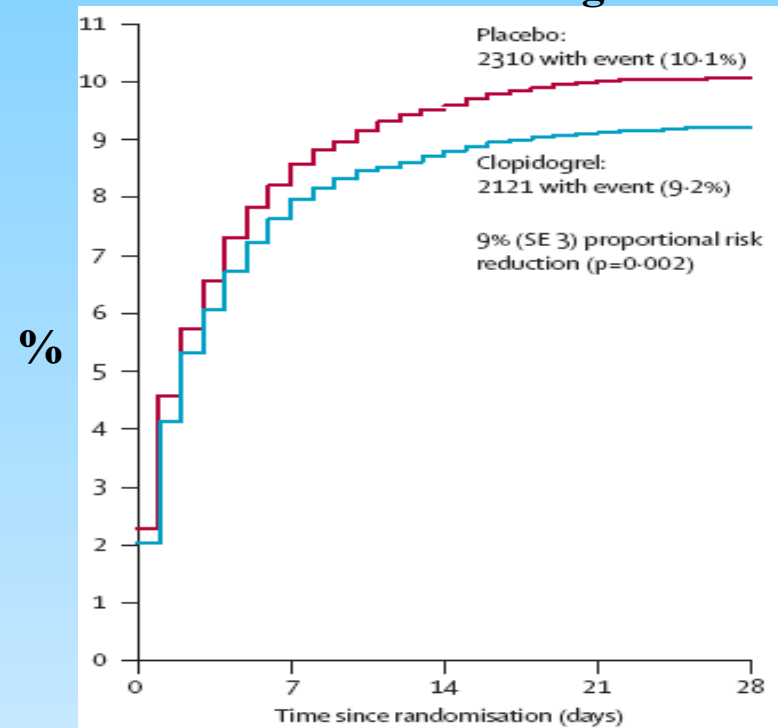


Sabatine et al. *N Engl J Med* 2005;352:1179-89.

COMMIT/CCS-2

n=46000

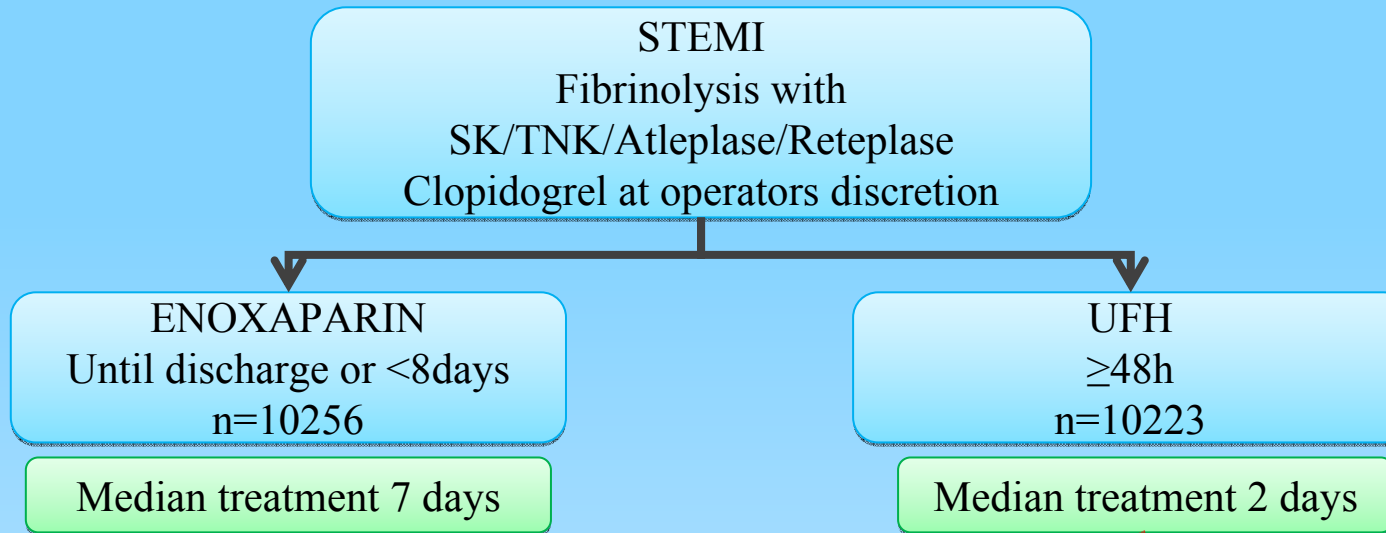
Death ReMI Stroke before discharge



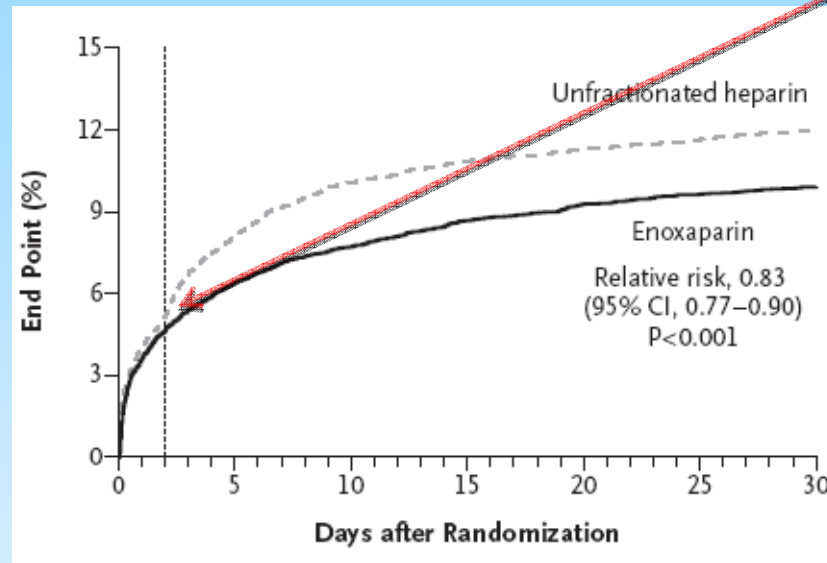
Bleeds ns

Lancet. 2005 Nov 5;366(9497):1607-21

LMWH in AMI: EXTRACT TIMI-25

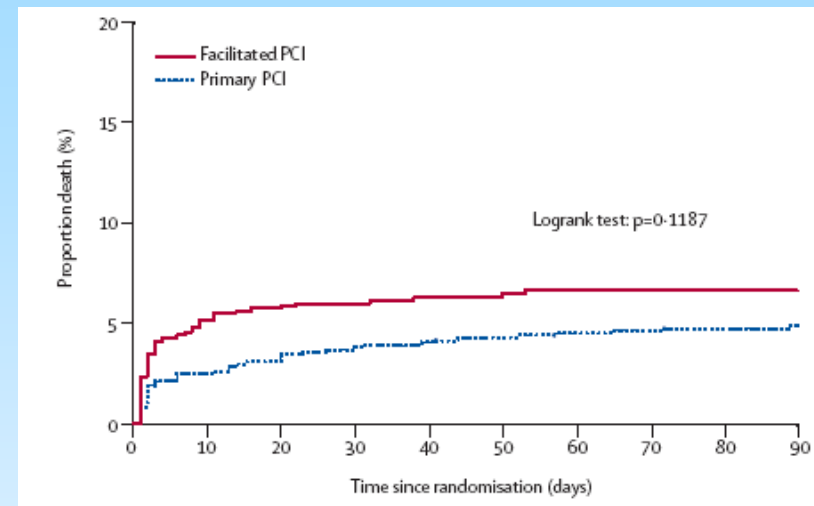
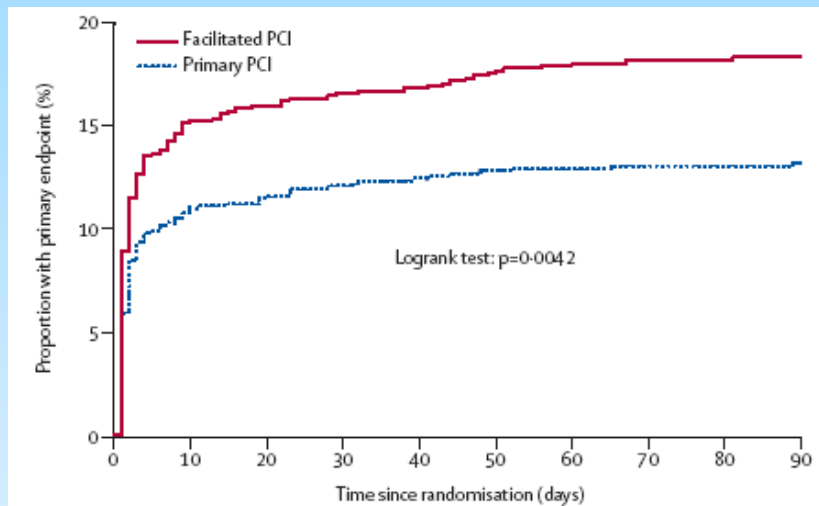
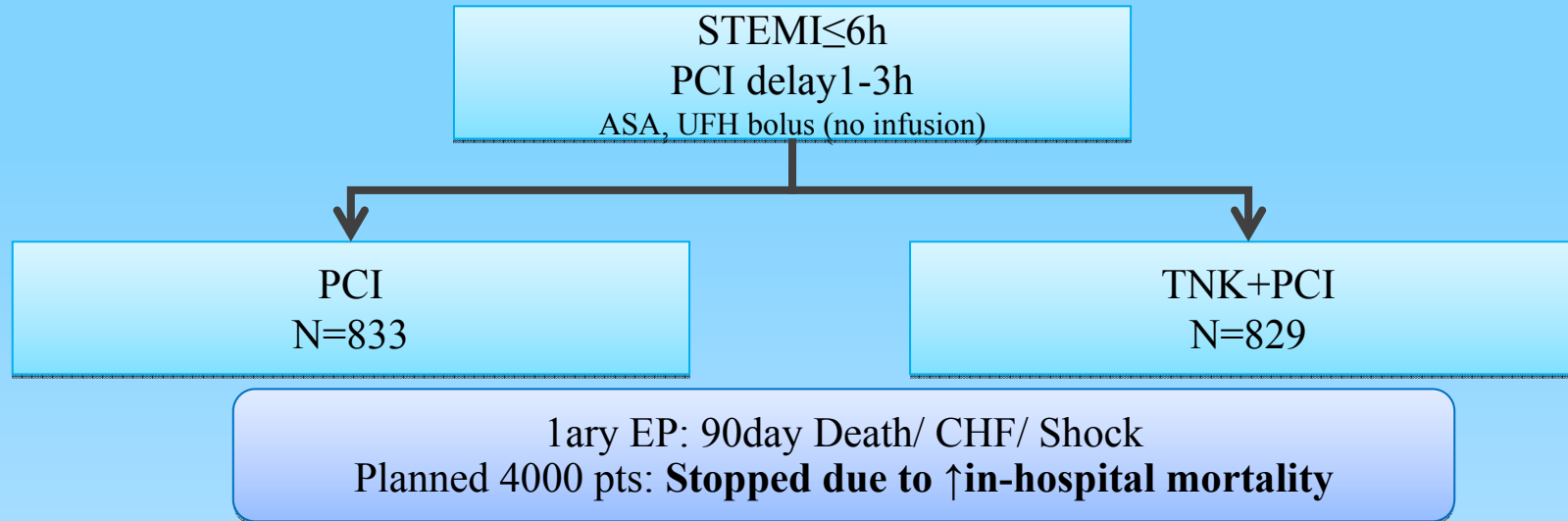


1ary EP=Death/ reMI
30days



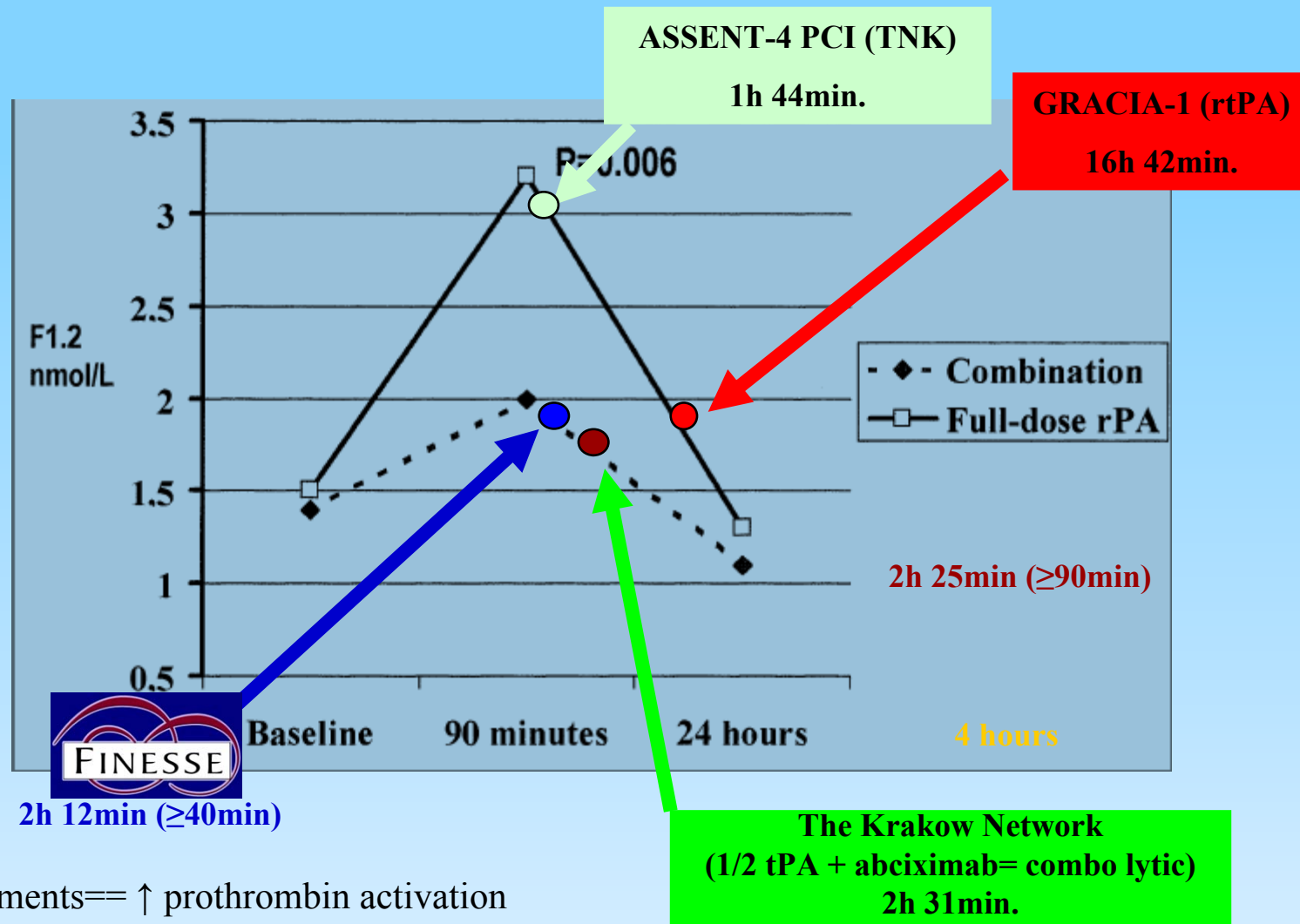
PHARMACOINVASIVE STRATEGIES IN ACUTE MI

ASSENT 4: Facilitated PCI

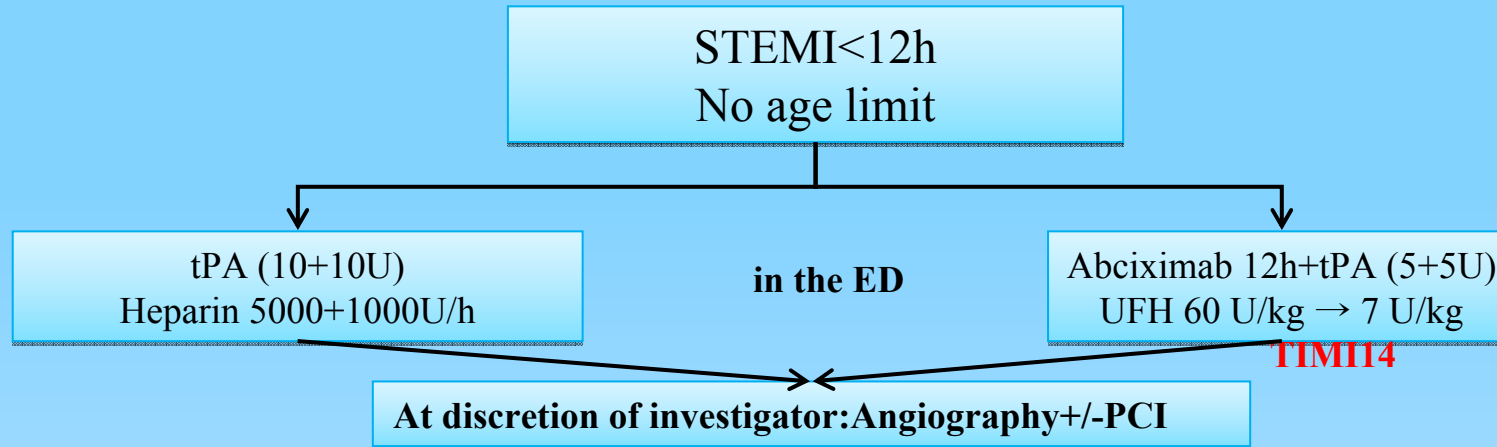


PHARMACOVASIVE STRATEGIES IN ACUTE MI

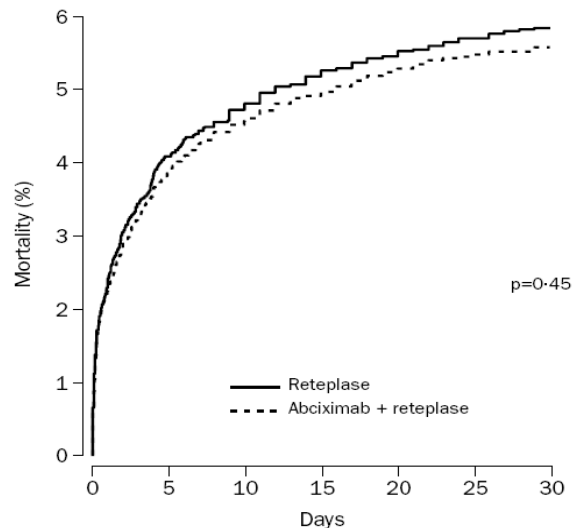
Prothrombotic effect of thrombolysis



GUSTO V

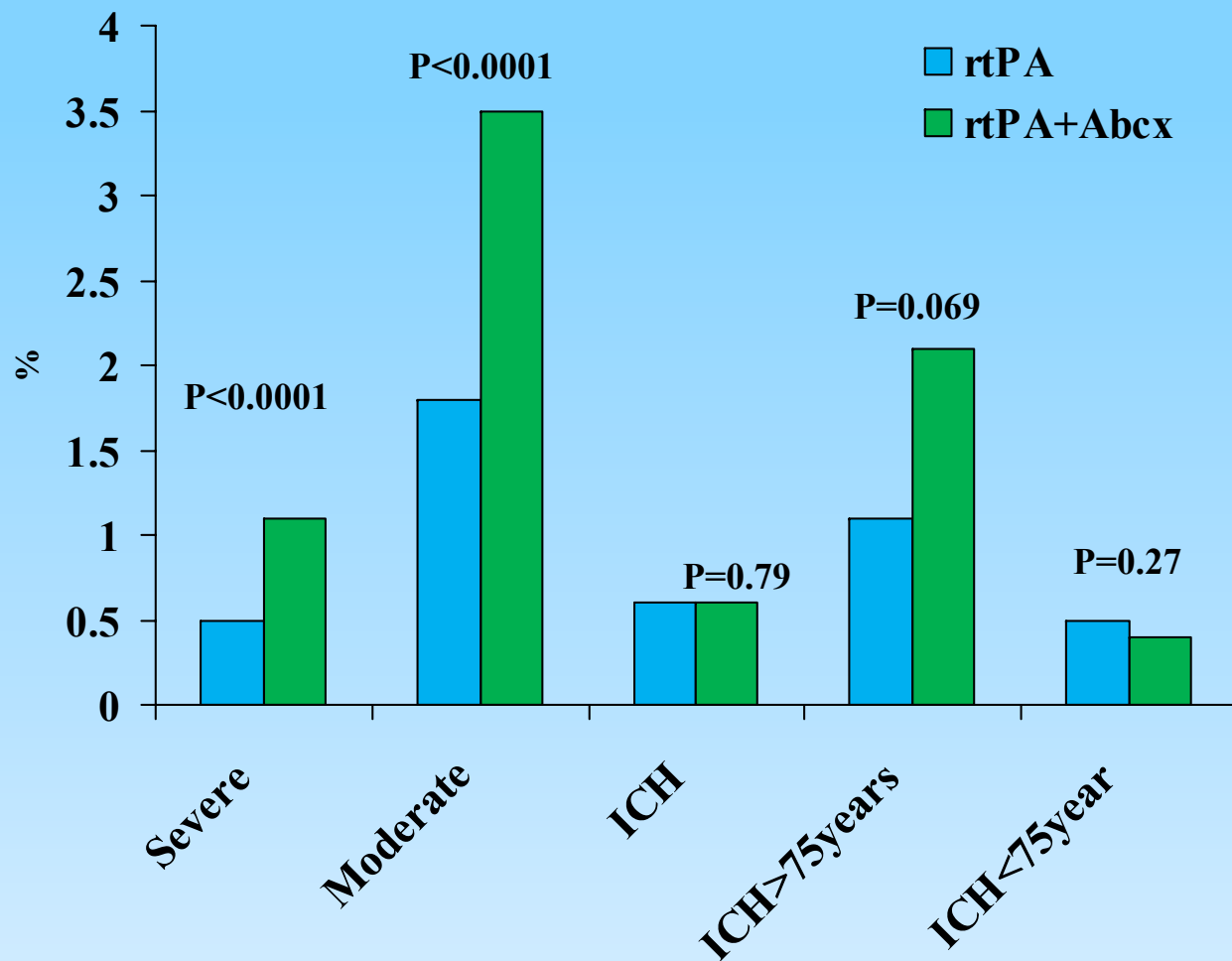


Primary EP: All-cause mortality
Safety EP: Severe Bleeding (hemodynamic compromise), moderate (transfusion), mild (other)



All-cause mortality at 30 days (5.9 vs 5.6%) test for superiority, $p=0.43$; for non-inferiority, relative risk 0.95 [95% CI 0.84–1.08].

GUSTO V: Bleeding





PHARMACOINVASIVE STRATEGIES IN ACUTE MI

Community
Hospital
Emergency
Department

'High Risk' ST Elevation MI within 12 hours of symptom onset

TNK + ASA + Heparin / Enoxaparin + Clopidogrel

Randomization stratified by age (≤ 75 vs. > 75) and by enrolling site

"Pharmacoinvasive Strategy"
Urgent Transfer to PCI Centre
N=522



"Standard Treatment"
N=508

Assess chest pain, ST \uparrow resolution
at 60-90 minutes after randomization

Failed Reperfusion*

Successful Reperfusion



PCI Centre
Cath Lab

Cath / PCI within 6 hrs
regardless of reperfusion
status



Cath and Rescue PCI \pm
GP IIb/IIIa Inhibitor

Elective Cath
 \pm PCI
>24 hrs later



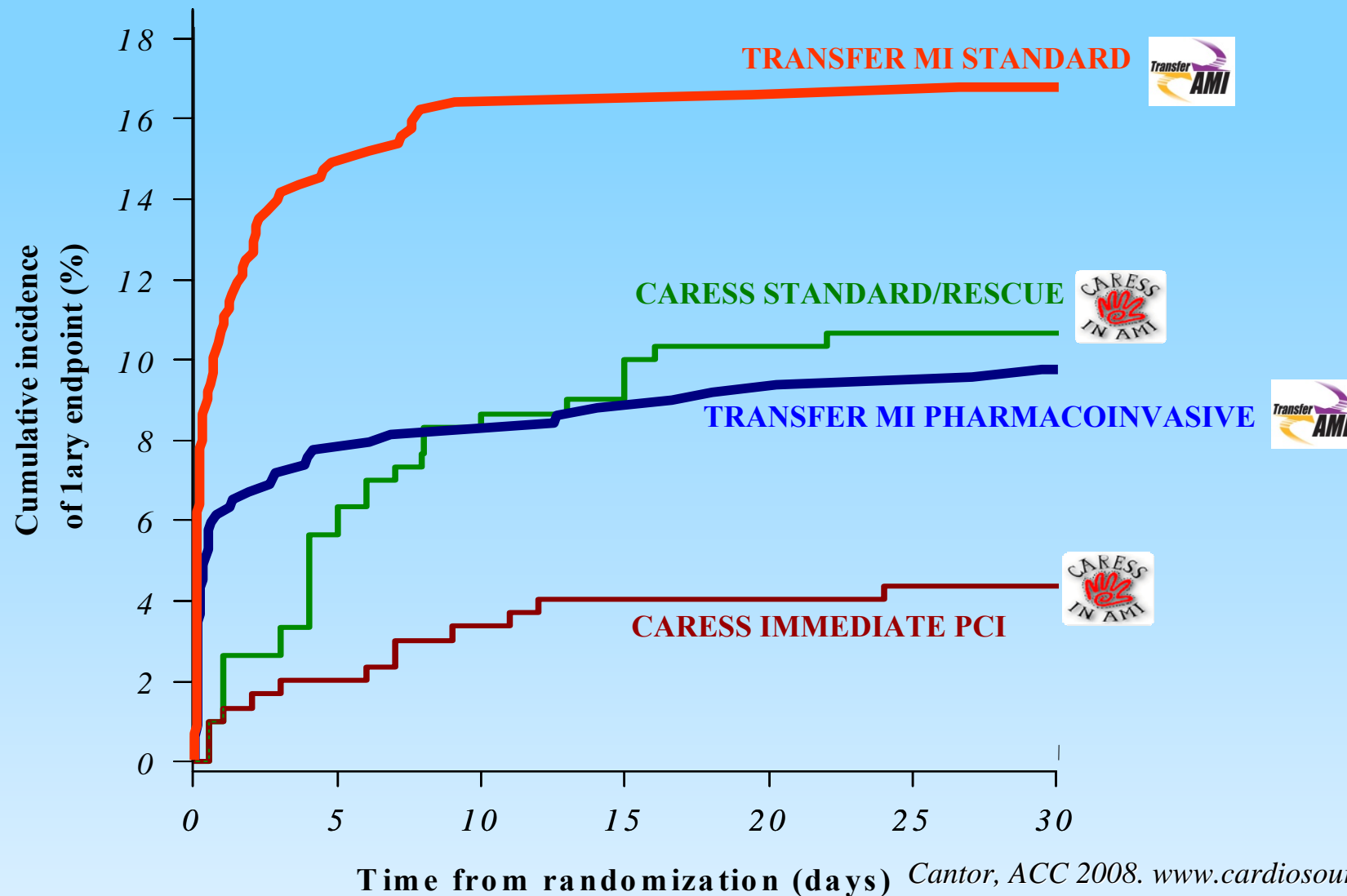
Repatriation of stable patients within 24 hrs of PCI

PCI within 12h from
thrombolysis=47%

* ST segment resolution < 50% & persistent chest pain, or hemodynamic instability

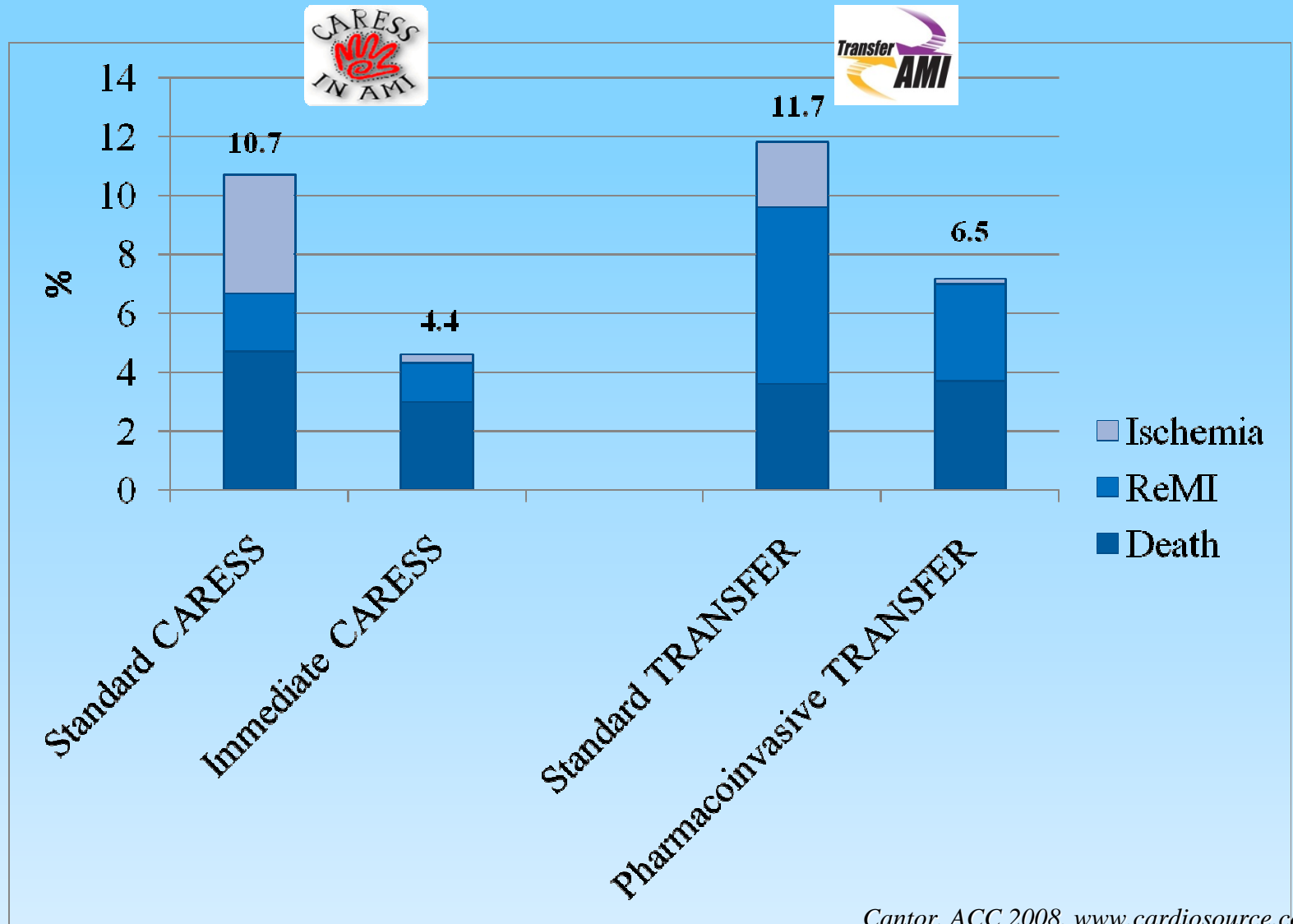
CARESS-in-AMI vs TRANSFER-MI

In TRANSFER-AMI endpoint included CHF + shock at 30 days



Cantor, ACC 2008. www.cardiosource.com
Di Mario et al. Lancet 2008;371:559-68

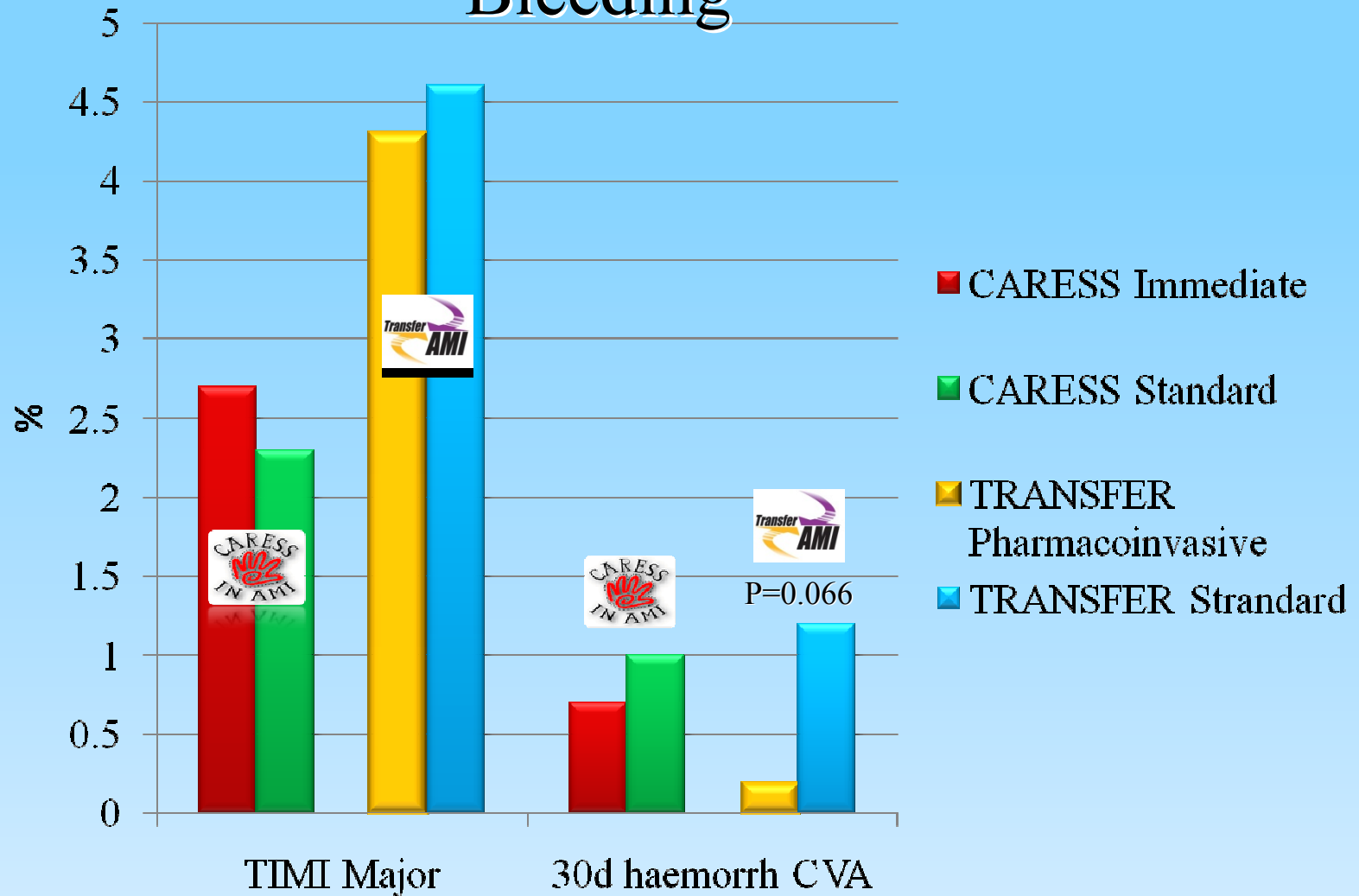
CARESS-in-AMI & TRANSFER-AMI



Cantor, ACC 2008. www.cardiosource.com
Di Mario et al. Lancet 2008;371:559-68




























CARESS-in-AMI & TRANSFER-AMI




Bleeding



PHARMACOINVASIVE STRATEGIES IN ACUTE MI

Pharmacologic strategies in AMI

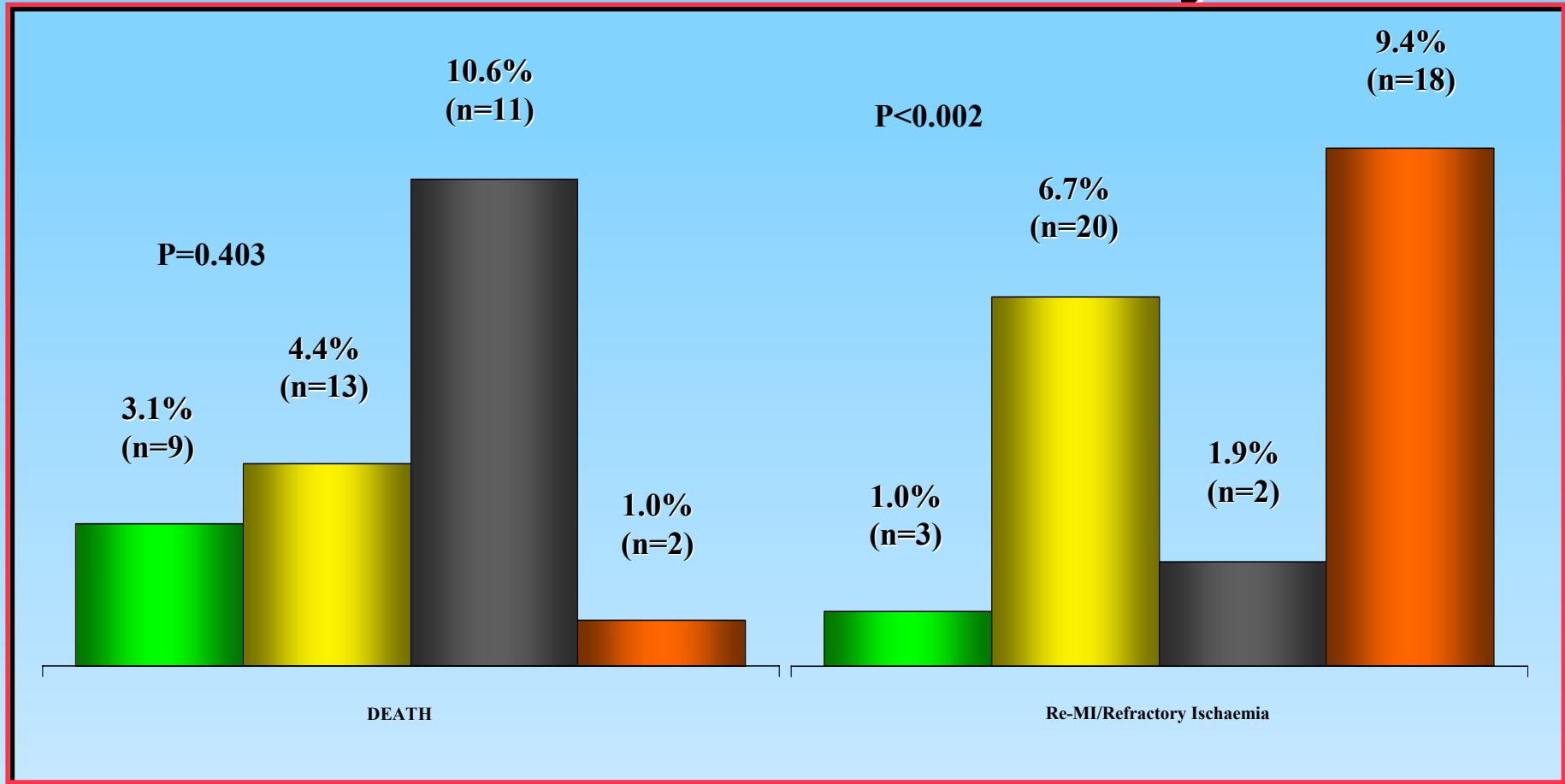
	Primary PCI possible within 90 minutes	Primary PCI NOT possible within 90 minutes
ANTIPLATELET		
- Aspirin		
- Clopidogrel		
- Prasugrel		
- Cangrelor		
- AZD6140		
- GP IIb/IIIa Inhibitors	 	
ANTITHROMBOTIC		
- UFH	 	 
- LMWH	 	
- Bivalirudin		
THROMBOLYTICS		
COMBINATION THERAPY (thrombolytics+GP IIb IIIa)		 



 Recommended  Under evaluation  Discouraged





Individual 30 day outcomes

Rescue/Medical Treatment Only Divided



 Facilitated PCI (n=294)
 Rescue PCI (n=106)

 Med. Treatment/ Rescue (n=298)
 Med. Treatment Only (n=192)