



ON-TIME-2

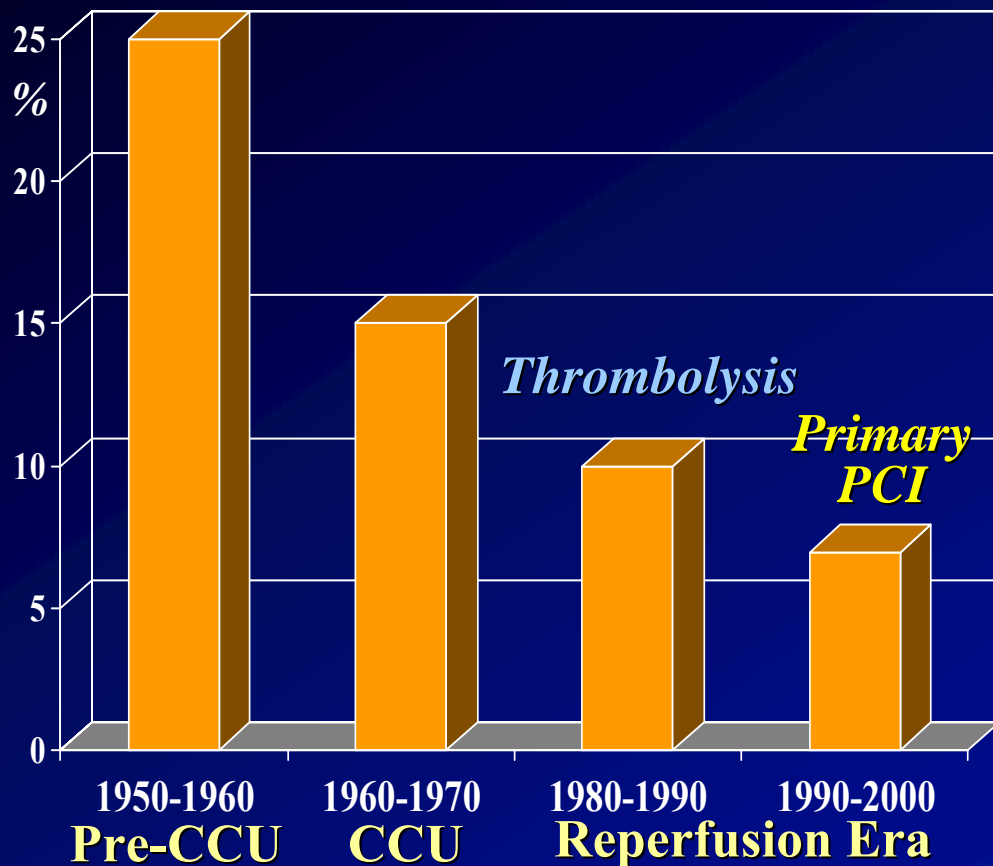
Ongoing **T**irofiban In **M**yocardial **I**nfarction **E**valuation

Harry Suryapranata
Isala Klinieken, Zwolle, The Netherlands
On behalf of the ON-TIME Study Group



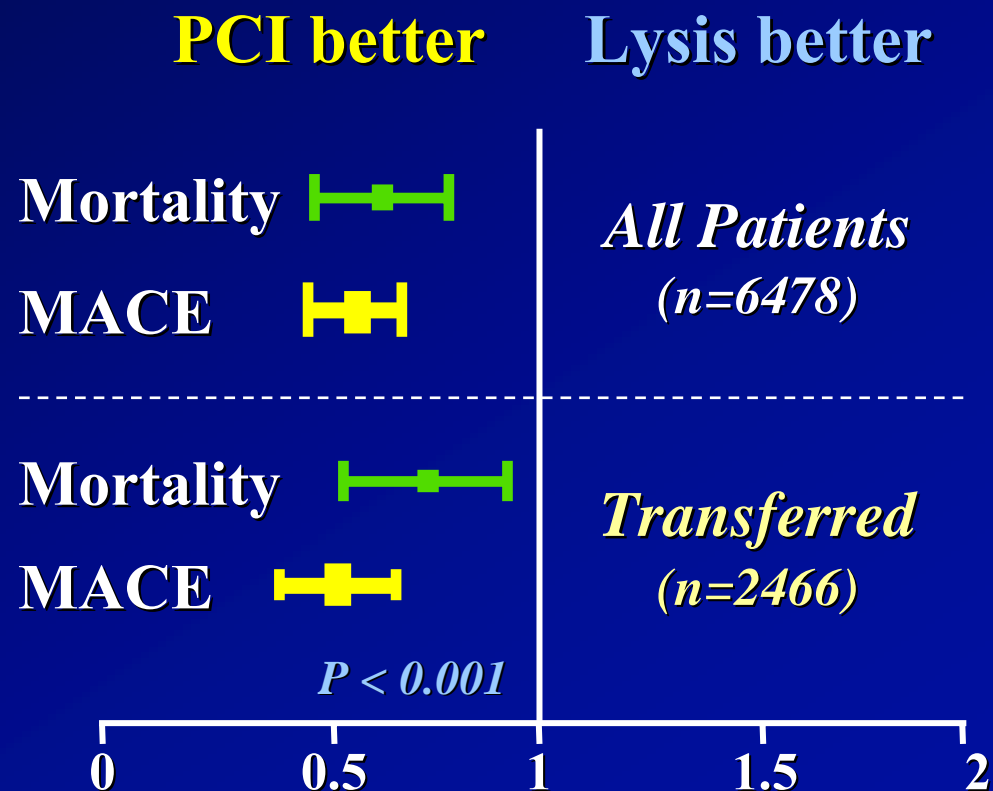
Reperfusion Therapy for STEMI

AMI Mortality Rate In The Netherlands



Source: Central Bureau for Statistics

Transferred for Primary PCI Pooled Analysis - OR (95% C.I)



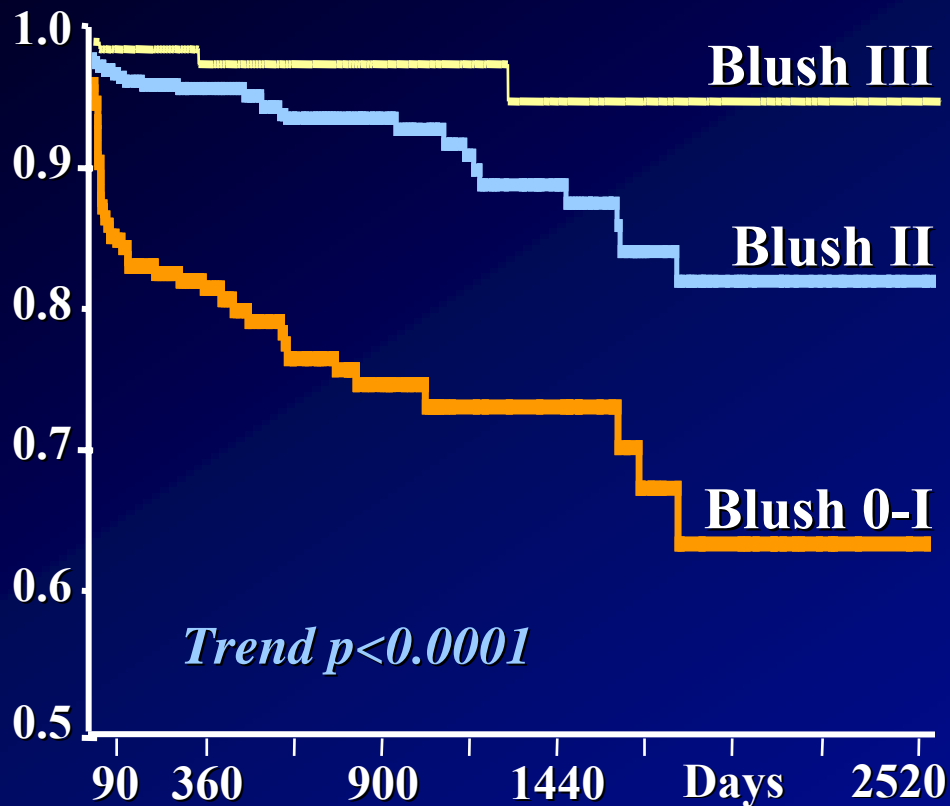
Zijlstra Eur Heart J 2003

PCI has never been shown to reduce Mortality, Except in subsets of AMI pts

Zwolle Randomized Trial

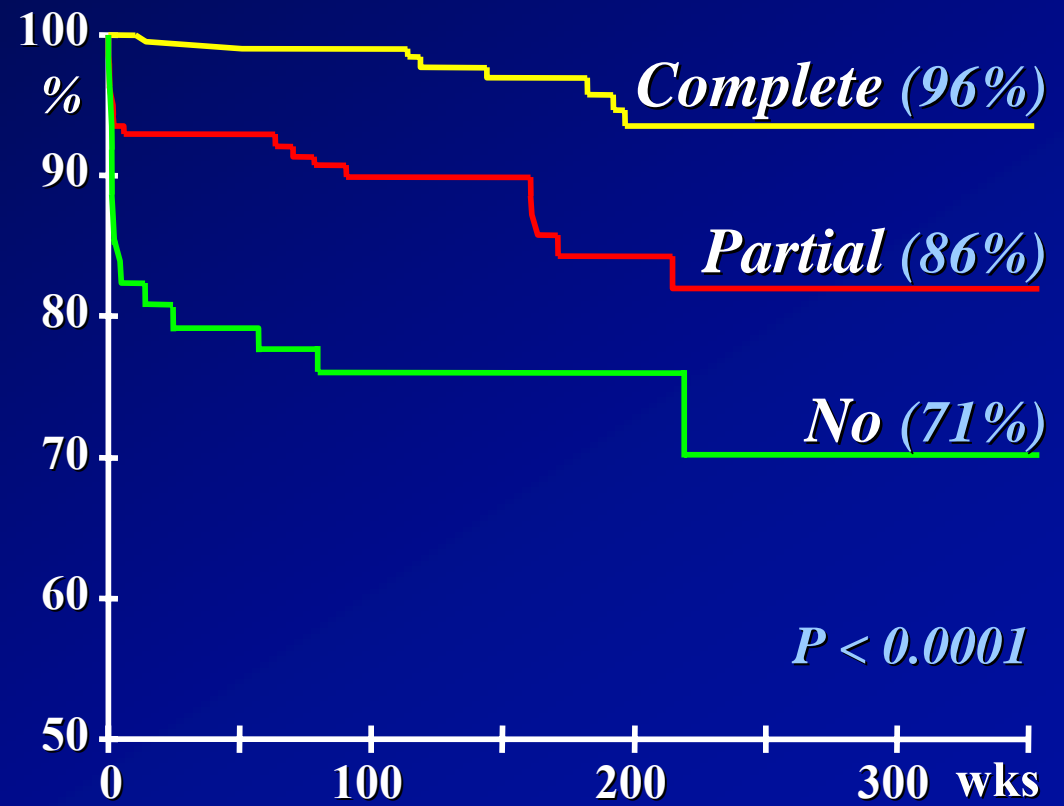
Sub-Optimal Myocardial Reperfusion - Long-term Outcome

MBG & Survival at 7 yrs



van 't Hof et al. Circulation 1998

ST-resolution & Survival at 7 yrs



van 't Hof et al. Lancet 1997

A simple pair of ECG and initial angiogram are effective in assessment of reperfusion success, and in predicting long-term clinical outcome

Predictors of Impaired Myocardial Perfusion

Pre-procedural TIMI-3: Independent determinant of survival

Zwolle Multivariate Analysis (n=1527)

Predictors *Odds Ratio [95% CI]*

Pre-TIMI 0/1 **2.65 [1.89-3.70]**

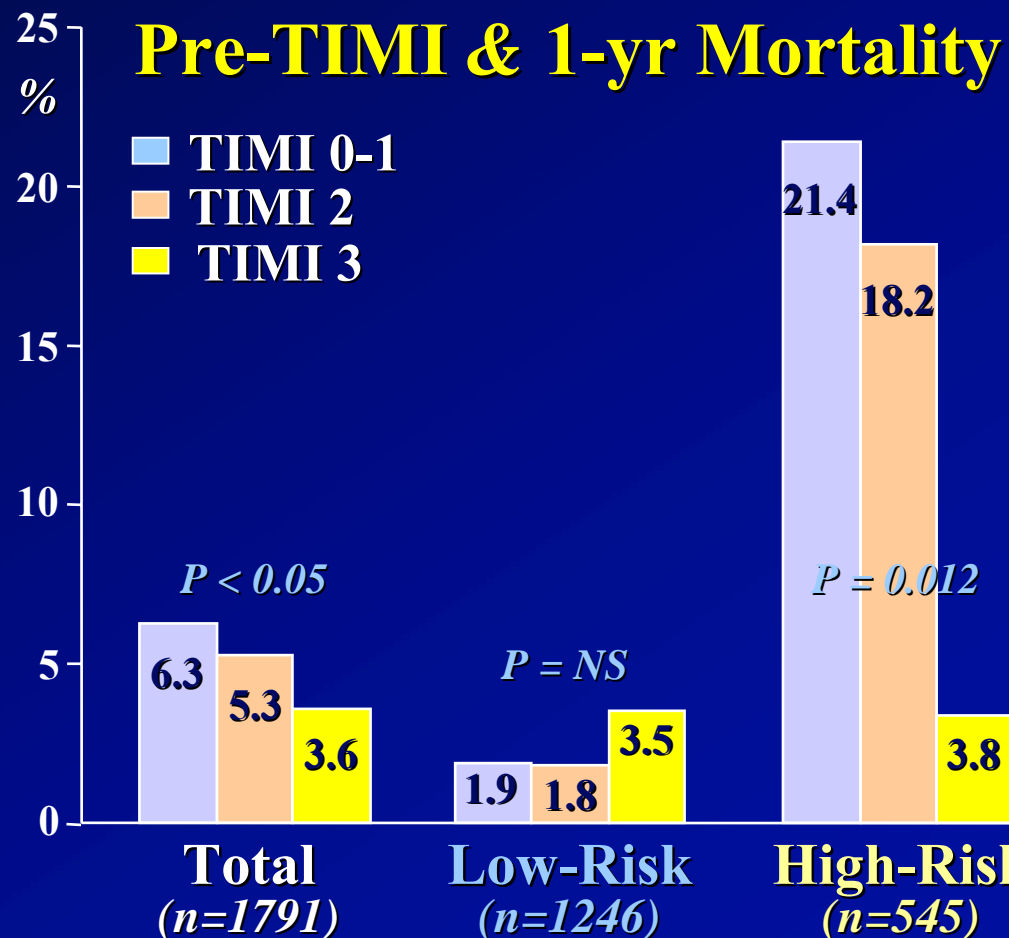
Anterior MI **2.15 [1.64-2.80]**

Time-delay (min) **1.06 [1.03-1.10]**

Killip class > 1 **1.78 [1.15-2.74]**

Age (yrs) **1.01 [1.00-1.02]**

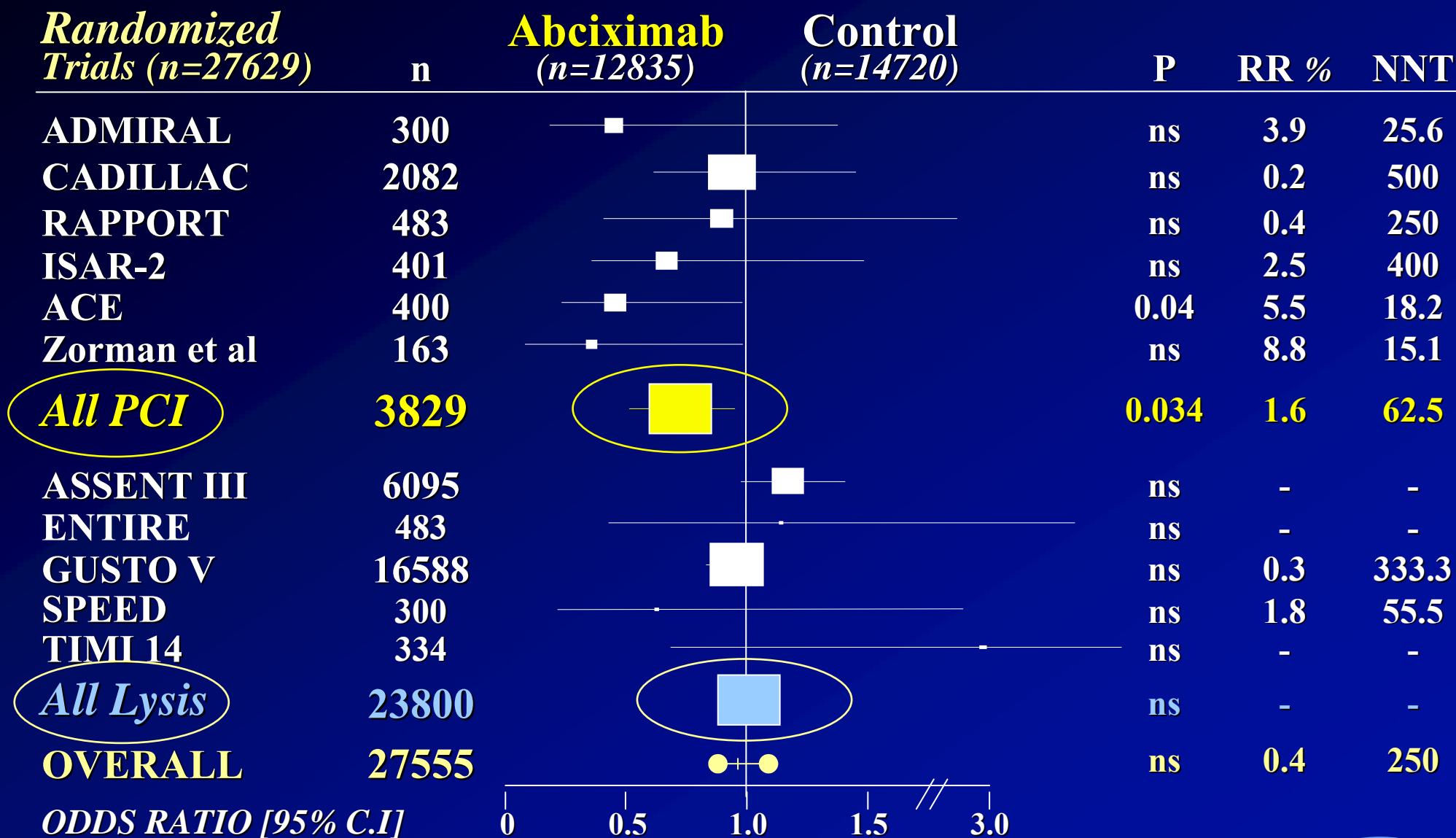
De Luca, Suryapranata et al. Am Heart J 2005



De Luca et al. JACC 2004

The need for EARLY TIMI-3 flow BEFORE PCI procedure

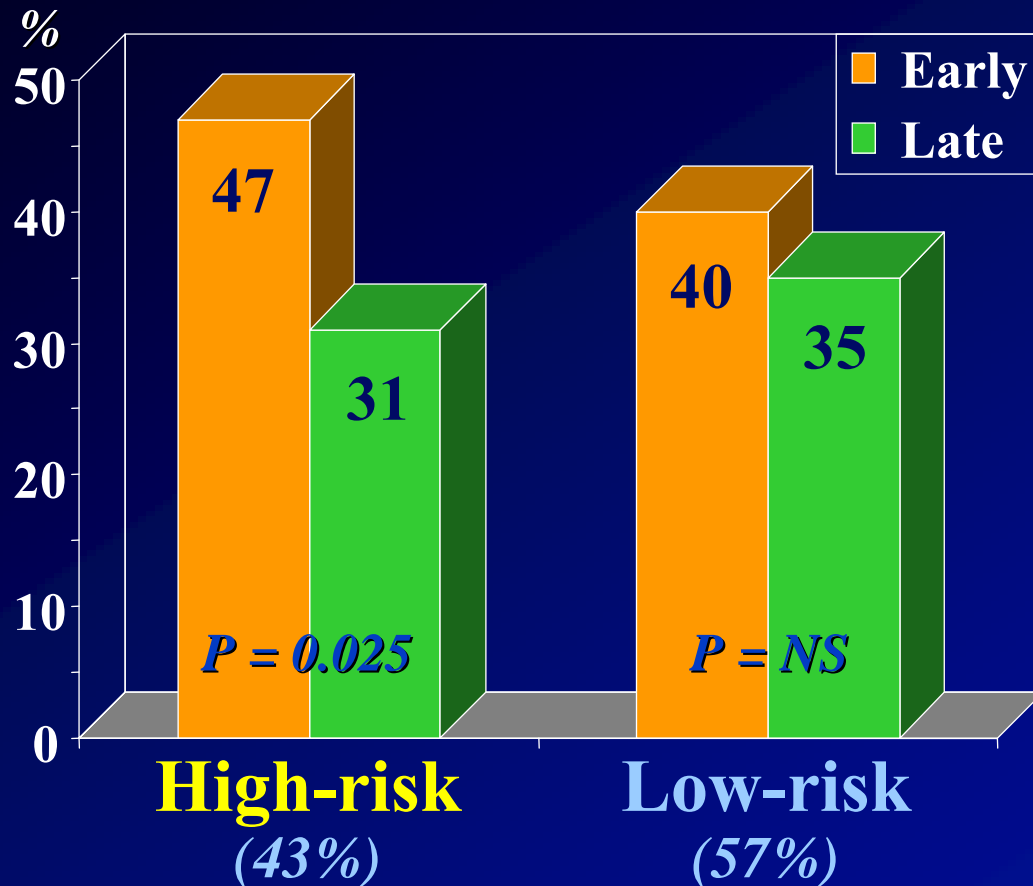
Meta-Analysis: Adjunctive I Ib/IIIa Inhibitor on 1-yr Mortality



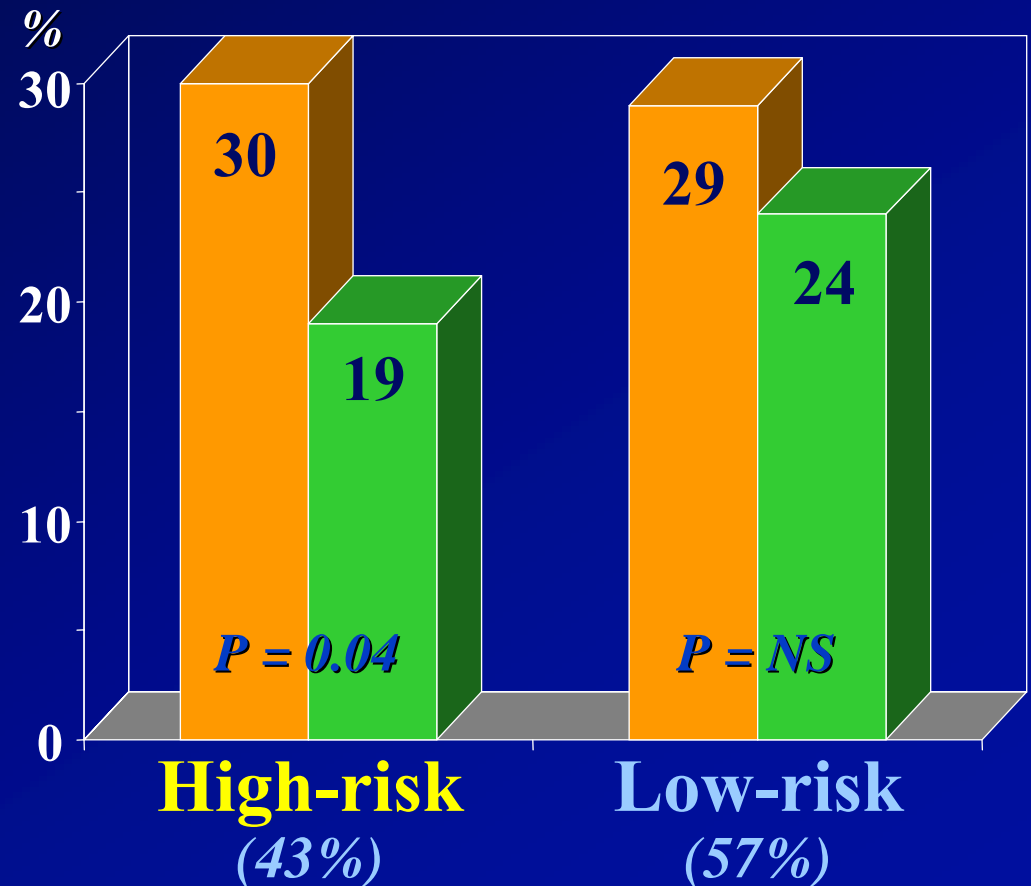
ONgoing Tirofiban In Myocardial Infarction Evaluation - 1

Early (Pre-hosp) vs Late (Cathlab) Tirofiban for STEMI

Initial TIMI 2/3



MBG 2/3

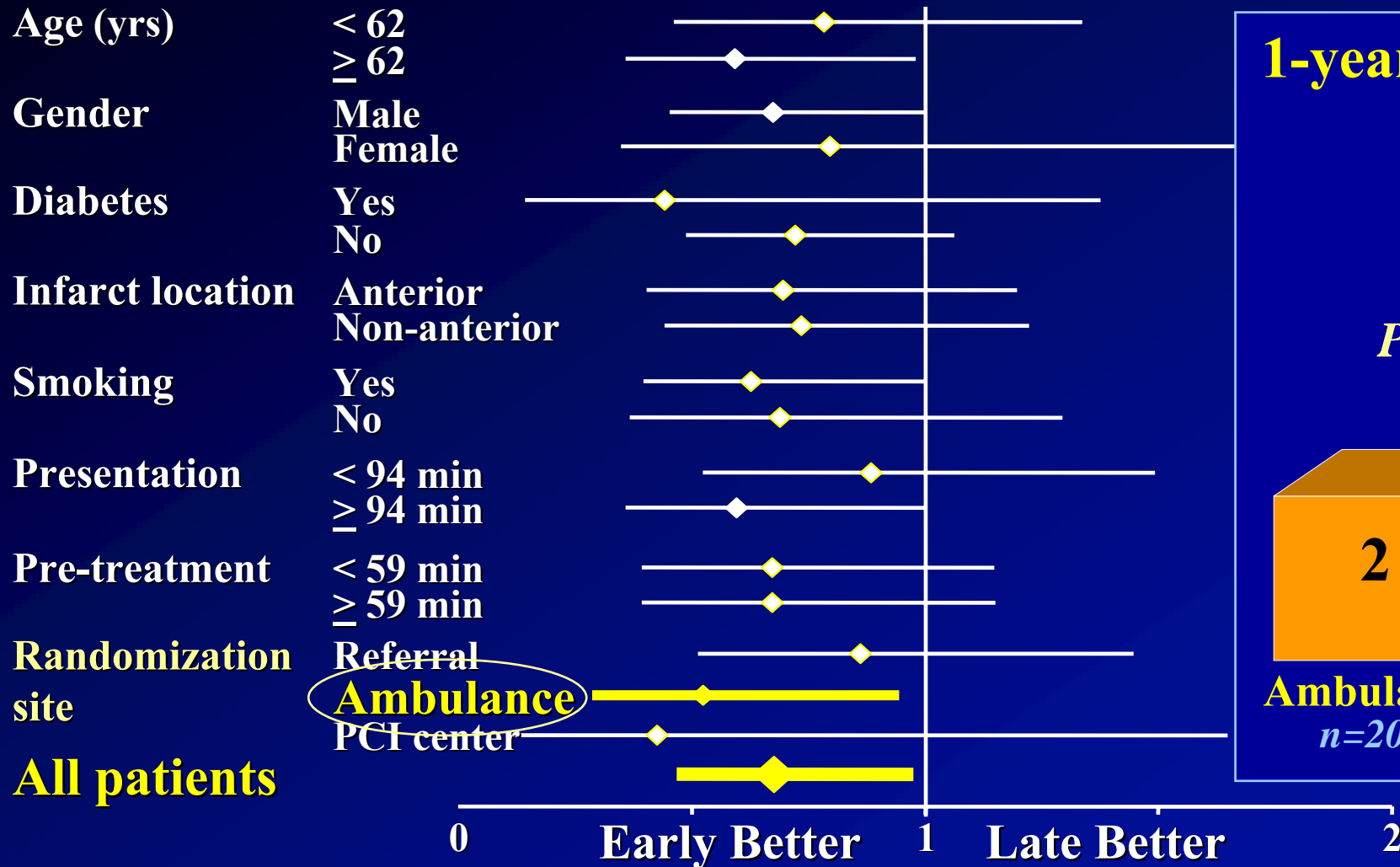


van 't Hof et al. Eur Heart J 2005

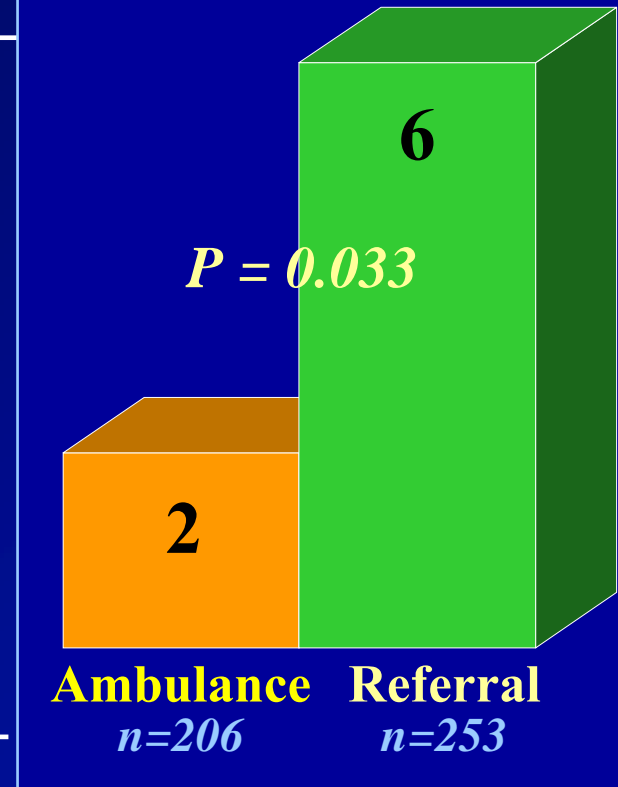
“The Higher The Risk - The Greater The Benefits”

ONgoing Tirofiban In Myocardial Infarction Evaluation - 1

Initial TIMI 2/3



1-year Mortality (%)



“The Early - The Better”



ON-TIME-2 Multicenter Randomized Trial

To assess safety & efficacy of high bolus Tirofiban vs Placebo on the extent of Myocardial Reperfusion in STEMI pts transferred for PCI

25 Participating Centers

The Netherlands:

- | | |
|----------------------------|------------------------|
| 1. Isala klinieken Zwolle | Dr. A.W.J. van 't Hof |
| 2. Antonius Nieuwegein | Dr. J. ten Berg |
| 3. UMC Utrecht | Drs. P.R. Stella |
| 4. Medisch Spectrum Twente | Dr. K. van Houwelingen |

Belgium:

- | | |
|-----------------------|-------------------|
| 1. AZ Sint-Jan Brugge | Dr. P. Coussement |
|-----------------------|-------------------|

Germany:

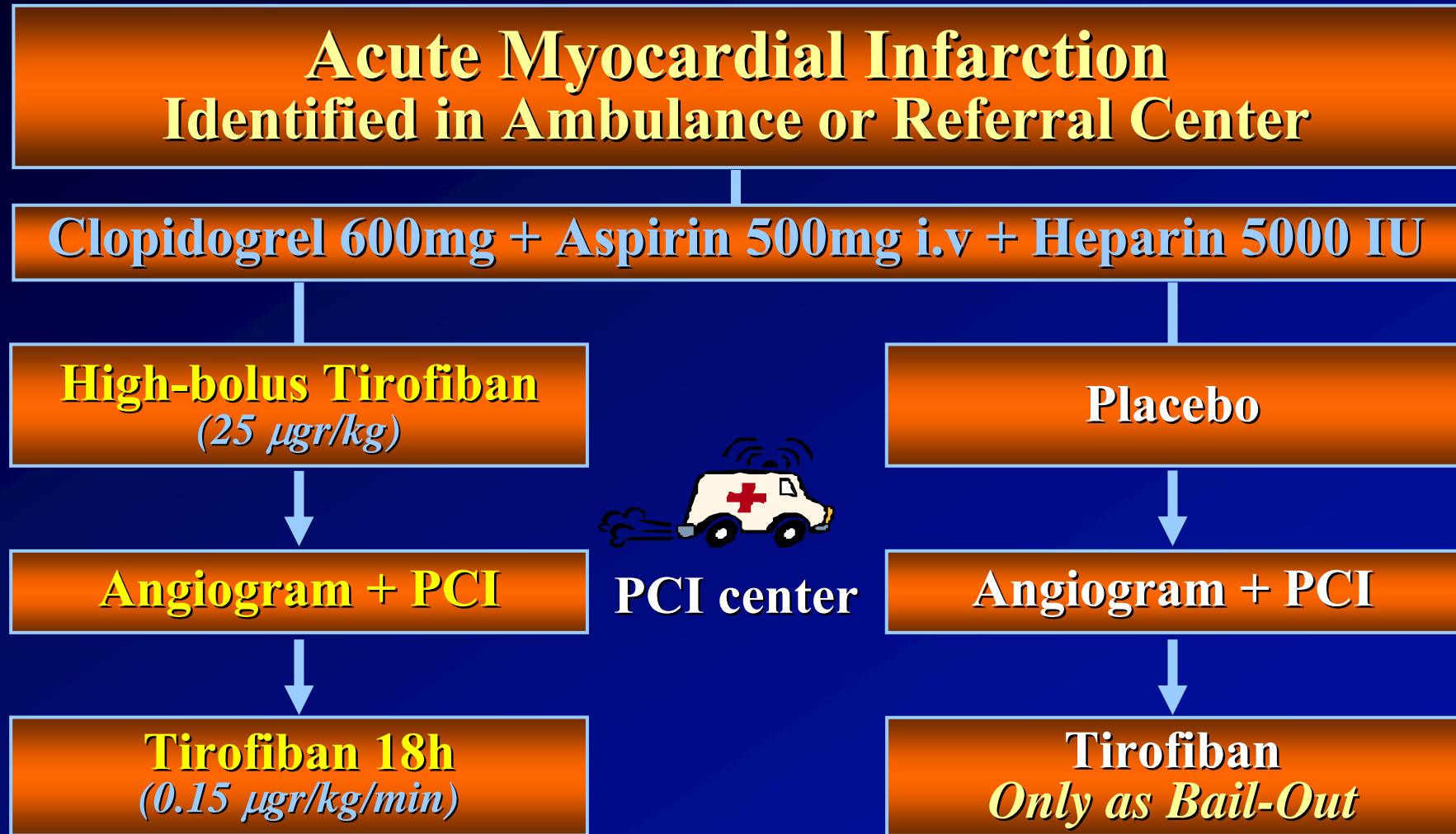
- | | |
|------------------------------------|------------------------|
| 1. Kerckhoff-Klinik | Prof. Dr. C. Hamm |
| 2. Universitätsklinikum Heidelberg | Prof. Dr. H Katus |
| 3. St. Johannes Hospital Dortmund | Prof. Dr. Heuer |
| 4. Klinikum Coburg | Prof. Dr. J. Brachmann |
| 5. Klinikum Lüdenscheid | Dr. Lemke |
| 6. Segeberger Kliniken | Prof. Dr. G. Richardt |
| 7. Philipps Universität Marburg | Prof. Maisch |
| 8. Allgemeines Krankenhaus Celle | Prof. Dr. W. Terres |
| 9. Uni-klinik Giessen | Prof. Dr. H. Tillmanns |
| 10. Imtalklinik Pfaffenhofen | Prof. C. Firschke |
| 11. Med. Hochschule Hannover | Prof. Dr. Schieffer |
| 12. Uniklinik Mannheim | Dr. T. Süsselbeck |
| 13. Uniklinik Lübeck | Prof. Dr. H. Schunkert |
| 14. Städtisches Klinikum Lüneburg | Prof. Dr. W. Kupper |
| 15. Zentralklinikum Suhl | Prof. W. Haberbosch |
| 16. Uni-Klinik Rostock | Prof. Dr. C.Nienaber |
| 17. Kreiskrankenhaus Bergstrasse | Dr. W. Auch-Schwelk |
| 18. Asklepios Klinik St. Georg | Prof. Dr. K.H. Kuck |
| 19. Klinikum Darmstadt | Prof Dr. G. Werner |
| 20. Evangelisches Holzminden | Dr. C. Beythien |

Presented at ACC, April 2008

June 2006 – November 2007: 984 pts enrolled

ON-TIME-2 Multicenter Randomized Trial

ONgoing Tirofiban In Myocardial Infarction Evaluation - 2



Study Endpoints

Primary:

- Residual ST-segment deviation ($>3mm$) 1 hr post-PCI

Key Secondary:

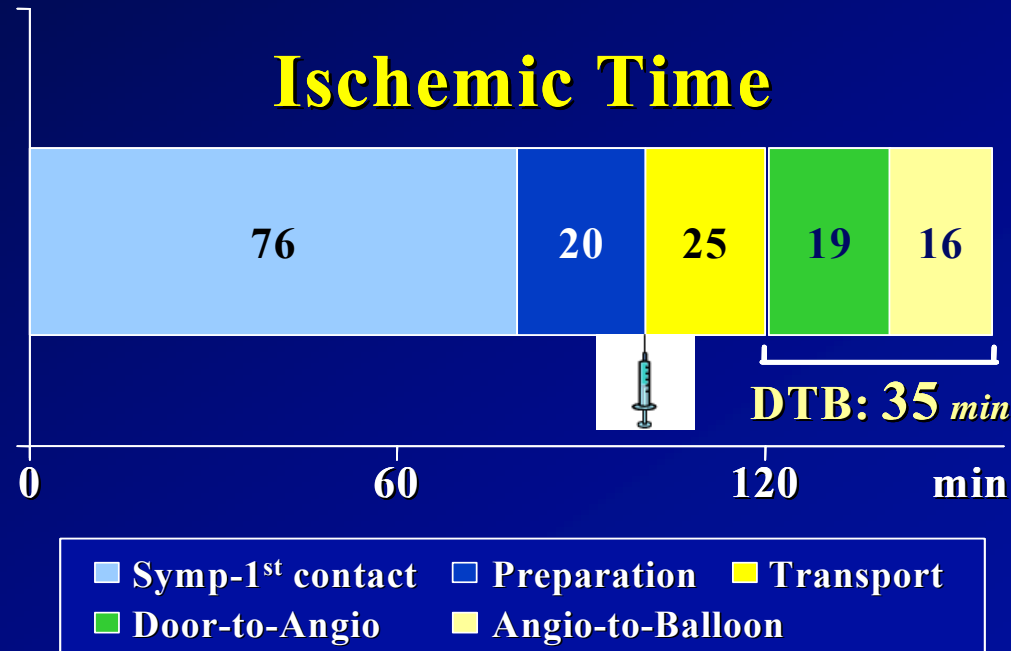
- Combined occurrence of Death, Re-MI, urgent TVR, or thrombotic Bail-out at 30 days follow-up
- Safety (major bleeding)



ON-TIME-2 Multicenter Randomized Trial

ONgoing Tirofiban In Myocardial Infarction Evaluation - 2

Baseline Data	Tirofiban (n=491)	Placebo (n=493)
Age (mean, yr)	62	62
TIMI risk >3 (%)	28	32
No AMI (%)	6	6
PCI performed (%)	88	90
CABG (%)	3	3
Conservative (%)	9	7
Symp-1 st contact (min)	72	79
Medication-Angio (min)	55	55
Transport distance (km)	25	25



Inclusion Site:

- Ambulance* **95%**
- Referral Hosp **3%**
- PCI Center **2%**

P=NS

* Without any physician on board

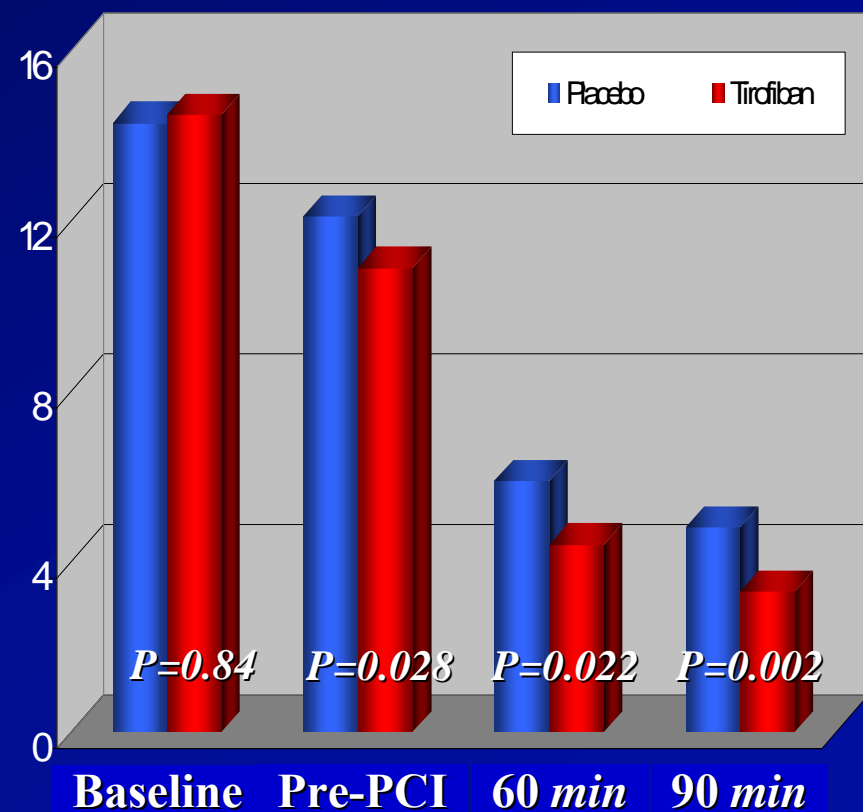
ON-TIME-2 Multicenter Randomized Trial

ONgoing Tirofiban In Myocardial Infarction Evaluation - 2

Primary Endpoint: Residual ST-Deviation >3mm

ECG and Angio Results	Tirofiban (n=491)	Placebo (n=493)	P
Readable ECG (%)	95.5	94.1	0.358
Residual ST-dev (mm)	3.3	4.8	0.002
ST-dev > 3mm (%)	36.6	44.3	0.026
Compl ST-Resol (%)	37.3	30.2	0.031
TIMI-flow 0-2 (%)	5.9	9.1	0.058
Abrupt closure (%)	0.2	2.2	0.004
Distal Emboli (%)	9.0	11.8	0.155

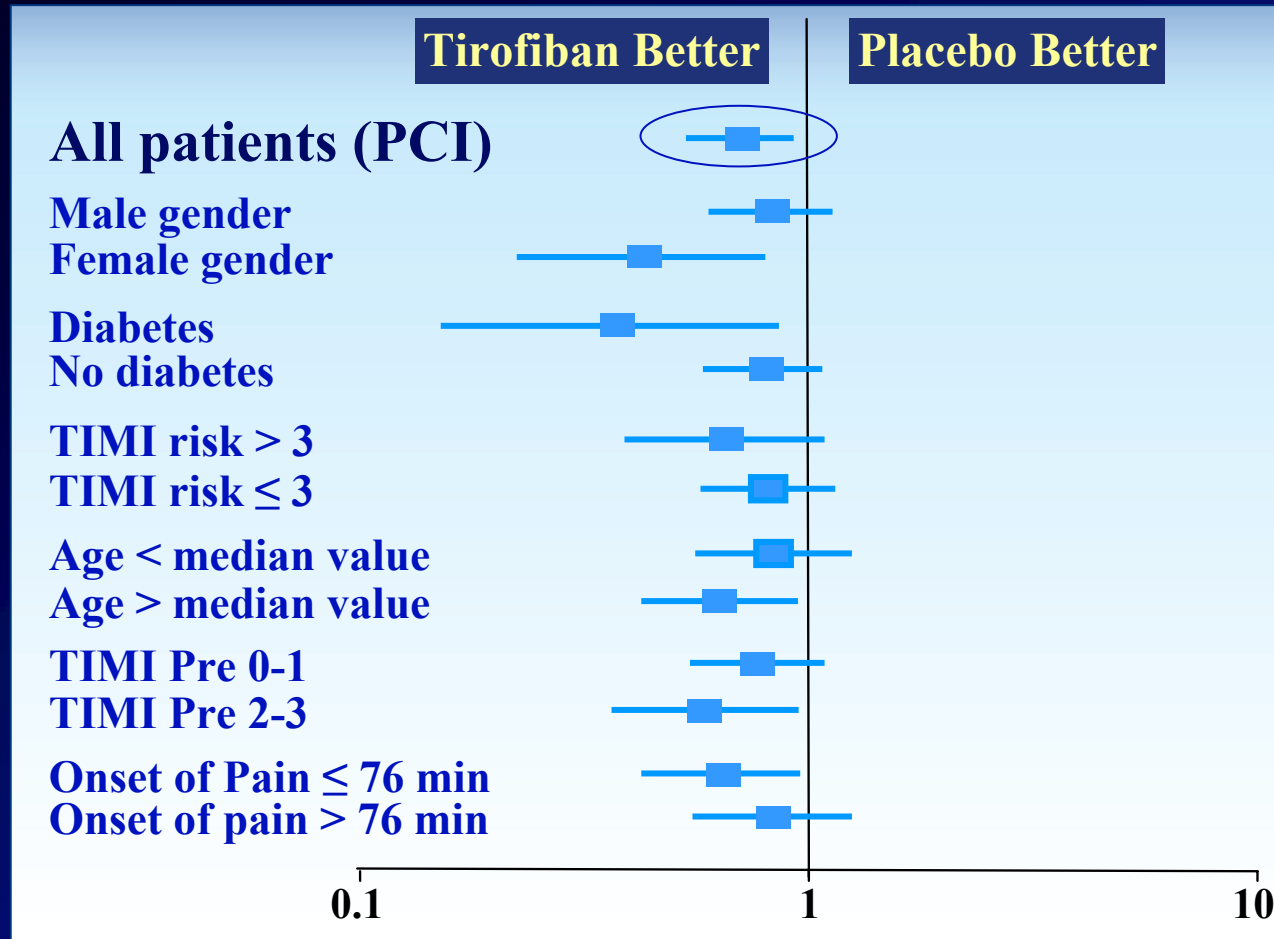
Cumulative ST-Deviation (mm)



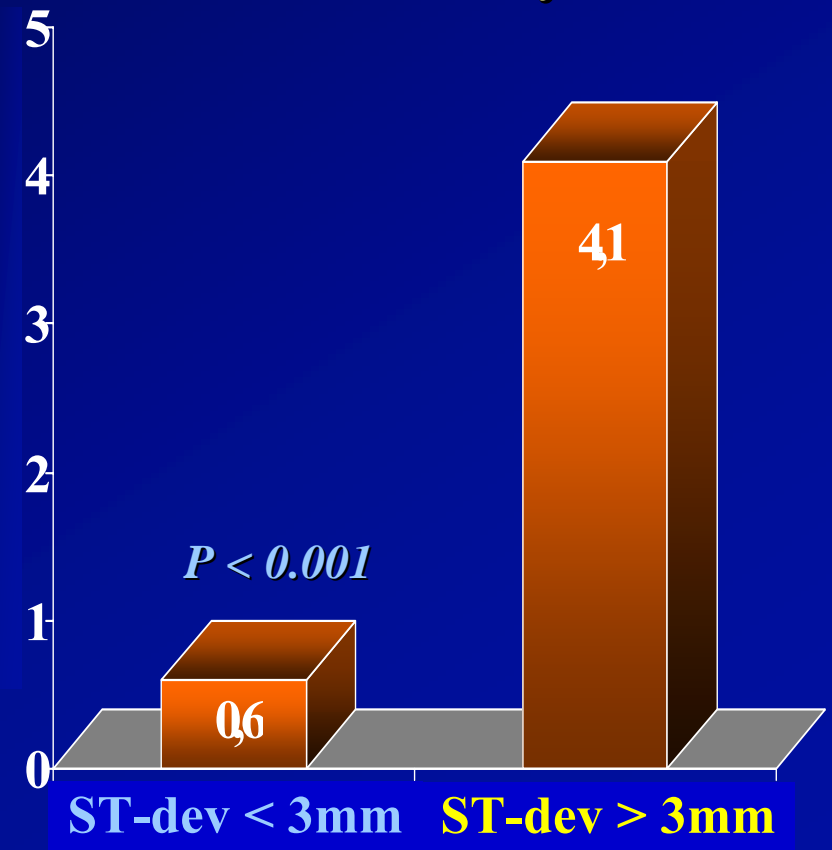
ON-TIME-2 Multicenter Randomized Trial

ONgoing Tirofiban In Myocardial Infarction Evaluation - 2

Primary Endpoint: Residual ST-Deviation >3mm



30-d Mortality (%)

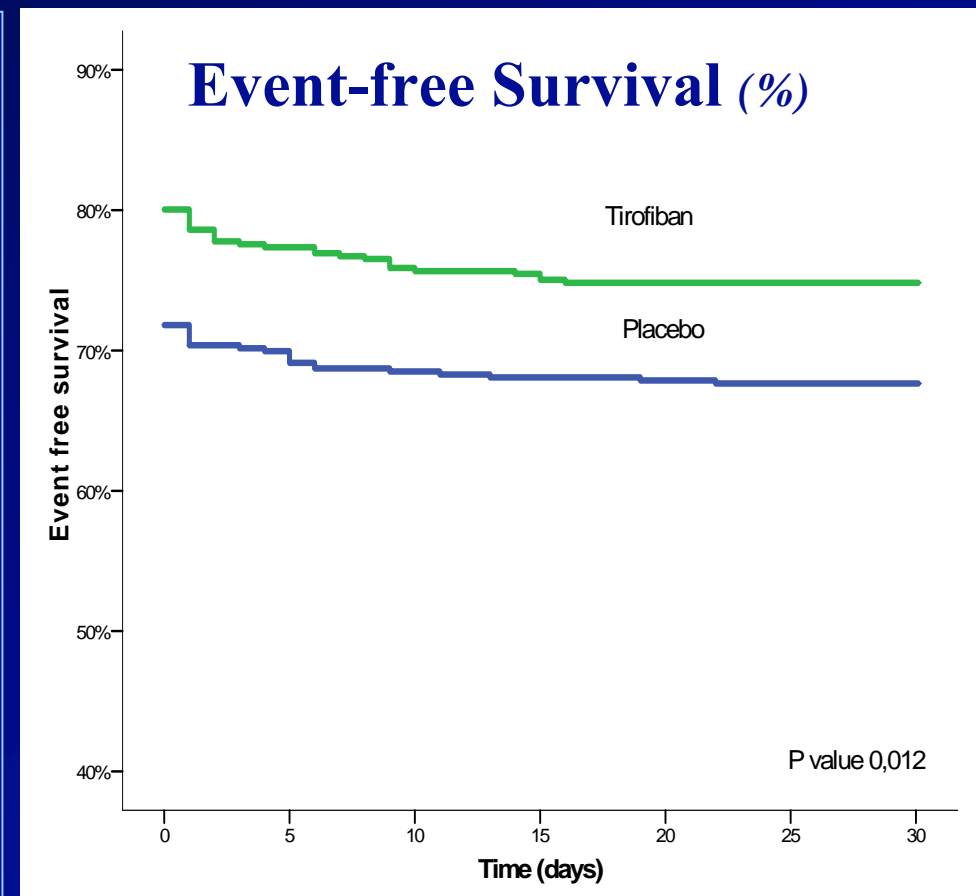


ON-TIME-2 Multicenter Randomized Trial

ONgoing Tirofiban In Myocardial Infarction Evaluation - 2

Secondary Endpoint: Clinical Outcome at 30-days

30-days Clinical F/U	Tirofiban (n=491)	Placebo (n=493)	P
Death (%)	2.3	4.0	0.144
Re-MI (mm)	2.7	2.9	0.863
Stroke (%)	0.2	1.5	0.069
Urgent TVR (%)	4.0	4.8	0.546
Bail-Out (%)	19.9	28.5	0.002
Bleeding (%)	4.0	2.9	0.363
Combined (%)	28.0	33.3	0.013



Conclusion

- Early initiation of a high-bolus Tirofiban (*on top of 600mg Clopidogrel*) in pre-hospital setting is safe and attractive for early facilitation of PCI in STEMI pts
- Improves ST-segment resolution before & after PCI
- Reduction in combined secondary clinical endpoint
- No increase in major bleeding complications
- Long-term Mortality benefit ?

