ST ELEVATION
MYOCARDIAL INFARCTION

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MAIN TOPICS

• Thrombolytic therapy
• Adjuncts to lysis
• Time to treatment
• Thrombolysis vs. angioplasty
• Transfer to PCI
• Adjuncts to primary PCI
• The approach to reperfusion
• Guidelines – based pharmacotherapy

DESIRED PROPERTIES OF NEW LYTIC AGENTS

• Faster, more complete, recanalization
• Less reocclusion
• Reduced bleeding risk
• ? Fibrin specificity
• Bolus administration
• Resistance to inhibitors (PAI-1)
• No immunogenicity
• Reduced cost

ASSENT - II

• 16,950 patients admitted within 6h.
• TNK-tPA bolus Vs front loaded tPA.
• 30d and 1 year follow up.

TNK-tPA

• A mutant of native t-PA with:
• Longer half life - bolus administration
• Increased fibrin specificity
• Resistance to PAI-1
**RETEPLASE (r-PA)**

- Deletion mutant of t-PA.
- Prolonged plasma clearance, double half life - bolus administration
- Less fibrin specific

**ASSENT-II**

<table>
<thead>
<tr>
<th></th>
<th>mortality</th>
<th>stroke</th>
<th>ICH</th>
<th>major bleeds</th>
</tr>
</thead>
<tbody>
<tr>
<td>tPA</td>
<td>0.9</td>
<td>1.8</td>
<td>0.9</td>
<td>1.8</td>
</tr>
<tr>
<td>TNK-tPA</td>
<td>0.9</td>
<td>1.8</td>
<td>0.9</td>
<td>1.8</td>
</tr>
</tbody>
</table>

**GUSTO III**

- 15,059 patients, ST ↑ AMI < 6h
- Double bolus reteplase front loaded t-PA
- 30 day mortality

**Comparison among equivalency analyses for 30-day mortality**

<table>
<thead>
<tr>
<th>Study</th>
<th>Time Interval</th>
<th>tPA</th>
<th>r-PA</th>
<th>Relative Difference</th>
<th>p value for equivalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>InTIME-2</td>
<td>30 min</td>
<td>6.77</td>
<td>6.50</td>
<td>-0.27</td>
<td>0.047</td>
</tr>
<tr>
<td>ASSENT 2</td>
<td>60 min</td>
<td>6.16</td>
<td>6.18</td>
<td>-0.02</td>
<td>0.005</td>
</tr>
<tr>
<td>GUSTO III</td>
<td>30 min</td>
<td>7.17</td>
<td>7.24</td>
<td>-0.07</td>
<td>ns</td>
</tr>
</tbody>
</table>

**STAPHYLOKINASE**

- Produced from transduced Staph. Aureus
- Readily inhibited by alpha-2 antiplasmin in plasma; hence - very fibrin specific
- When given as a double bolus (15 mg each 30 min apart), TIMI 3 flow achieved in 68%.
- Neutralizing antibodies produced.
- At least equivalent to t-PA
**Deficiencies of current fibrinolytic regimens for STEMI**

- Suboptimal macroperfusion
  - ± 60% TIMI grade 3 flow at 90 min
- Inadequate microperfusion
  - Impaired tissue flow in > 50% of pts with TIMI grade 3 flow
- High rates of reocclusion
  - Inhospital reinfarction ± 4%
- High rates of ICH
  - 0.5 – 1.0%
  - Angiographically proven reocclusion ± 25% at 3 months

**LMWH and fibrinolysis**

- Reocclusion TIMI 3 ± 0.1
- Late patency TIMI 3
- Reinfarction
- Infarction

**UFH post lysis**

- Bolus: 60 U/Kg, maximum of 4000U.
- Infusion: 12 U/Kg/h, up to 1000u/h
- aPTT target: 50-70 sec.
- aPTT>70 sec. associated with increased mortality
- After tPA- give 24-48 hours. After SK -?
- Weight adjustment probably reduces bleeding complications

**AMI-SK**

**Safety at day 30**

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Enoxaparin</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 239)</td>
<td></td>
<td>(n = 252)</td>
<td></td>
</tr>
<tr>
<td>Major bleed (%)</td>
<td>2.5</td>
<td>4.8</td>
<td>0.2</td>
</tr>
<tr>
<td>ICH (%)</td>
<td>0.4</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>↓ Hb ≥ 3 g/dL (%)</td>
<td>2.1</td>
<td>4.4</td>
<td></td>
</tr>
<tr>
<td>Transfusion ≥ 2 U (%)</td>
<td>1.3</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>TIMI major bleed (%)</td>
<td>0.8</td>
<td>1.6</td>
<td></td>
</tr>
<tr>
<td>Any stroke (%)</td>
<td>1.3</td>
<td>—</td>
<td>0.1</td>
</tr>
</tbody>
</table>

**Study design (2)**

- Suspected MI, < 12 h, ST ↑
- Enoxaparin
  - 30 mg IV bolus + 1 mg/kg SC q12 h
  - 3 x d (range: 3 – 8 d)
  - GP IIb/IIIa RAs only permitted if PCI performed
- Placebo
  - Angiography day 8
  - (range: 5 – 10 d)

**HART II**

**Design**
- STEMI < 12 h (n = 400)
- Aspirin and accelerated alteplase
- Enoxaparin 30 mg IV bolus + 1 mg/kg SC q12 h x ≥ 72 h
- UFH 5,000 IU bolus + 15 IU/kg/h IV infusion x ≥ 72 h (adjusted to aPTT)
- Angiography at 90 min
- Repeat angiography at 5 – 7 days

**AMI-SK**

**Efficacy**

<table>
<thead>
<tr>
<th>Clinical events at day 30</th>
<th>Placebo</th>
<th>Enoxaparin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of patients</td>
<td>7.0</td>
<td>6.7</td>
</tr>
<tr>
<td>00</td>
<td>10</td>
<td>7.0</td>
</tr>
<tr>
<td>10</td>
<td>13</td>
<td>7.4</td>
</tr>
<tr>
<td>20</td>
<td>15</td>
<td>7.6</td>
</tr>
</tbody>
</table>

**HART II**

**Reocclusion within 1 week**

<table>
<thead>
<tr>
<th>Percentage of patients</th>
<th>UFH</th>
<th>Enoxaparin</th>
</tr>
</thead>
<tbody>
<tr>
<td>00</td>
<td>10</td>
<td>7.0</td>
</tr>
</tbody>
</table>

**HART II**

**Infarct artery patency at 90 minutes**

<table>
<thead>
<tr>
<th>Percentage of patients</th>
<th>UFH</th>
<th>Enoxaparin</th>
</tr>
</thead>
<tbody>
<tr>
<td>00</td>
<td>10</td>
<td>7.0</td>
</tr>
</tbody>
</table>

**ASSENT-3**

**1º efficacy endpoint**

Probability of event (%)

Log-rank test: P = 0.0001

Days to death or inhospital reinfarction or refractory ischemia

**ASSENT-3**

**Design**

- STEMI < 6 h
- UFH IV bolus
- Enoxaparin IV bolus
- Abciximab IV bolus
- TNK-4PA full-dose IV bolus

- Enoxaparin SC q12 h up to discharge or revascularization (max of 7 d)
- Abciximab IV infusion for 12 h
- Reduced weight-adjusted UFH for up to 48 h
ASSENT-3

Conclusions (1)

- Both enoxaparin and abciximab, given in conjunction with single bolus TNK-tPA, significantly reduce the frequency of ischemic complications of AMI.
- Taking into account efficacy and safety, the ease of administration and the lack of need for monitoring anticoagulation, the combination enoxaparin and TNK-TPA emerged as the best treatment.


ASSENT-3 PLUS

- Pre hospital enoxaparin vs. UFH with TNK-tPA
- Overall — similar, but increased bleeding and ICH in patients > 75 with enoxaparin
- Enoxaparin may not be suitable with lysis >75, especially in the pre hospital setting.

EXTRACT-TIMI 25

Protocol design

- STEMI < 6 h
- Lytic eligible
- Enoxaparin: 30 mg IV bolus 1.0 mg/kg SC q 12 h to hosp DC
- UFH: Bolus 60 U/kg Infusion 12 U/kg/h x > 48 h

Day 30

1° efficacy endpoint: MI / refractory ischemia / ICH / major bleeding

1° safety endpoint: TIMI major hemorrhage / ICH / major bleeding

Double-blind

Lytic choice by MD

Post hoc stratified analysis

ASA

 Trials of anticoagulant agents

- Limited (if any) role during initial lysis process
- Eg: TAMí-3, GUSTO I
- Critically important to prevent early recirculation/re-MI
- In comparison with UFH, fewer re-MIs due to
  - More complete lysis of thrombus (direct antithrombins)
  - Less generation of new thrombin (LMWH)
  - More stable and prolonged anticoagulant effect (LMWH)
- However, no survival benefit but trend towards more bleeding complications

Direct thrombin inhibitors: meta-analysis in ST ↑ ACS (n=35 970)

- OR: 1.67 (0.88–1.11)
- OR: 0.75 (0.55–0.94)
- OR: 0.91 (0.77–1.06)

- Direct thrombin inhibitor vs. control

**ENTIRE-TIMI 23**

**Design**

STEMI < 6 h

**Standard reperfusion:**
- Full-dose TNK-TPA (0.53 mg/kg)

**Combination reperfusion:**
- Abciximab + 1/2-dose TNK-TPA (0.27 mg/kg)

**UFH**
- Bolus: 50 U/kg
- Infusion: 7 U/kg/h ≥ 36 h

**Enoxaparin**
- Bolus: 40 U/kg
- Infusion: 7 U/kg/h ≥ 36 h

**Outcomes**
- 1st endpoints: TIMI 3 flow at 60 minutes; TIMI major hemorrhage at 30 d
- 2nd endpoints: ST resolution; ischemic events

**UFH**
- Bolus: 60 U/kg
- Infusion: 12 U/kg/h ≥ 36 h

**Enoxaparin**
- IV bolus
- Index hosp (8 d)

**Combination reperfusion:**
- Abciximab + 1/2-dose TNK-TPA (0.27 mg/kg)

**STEMI < 6 h**

**Full-dose TNK-TPA**
- tPA + abciximab + UFH
- tPA + abciximab + ENOX + UFH

**Half-dose TNK-TPA + abciximab**
- tPA + UFH
- tPA + ENOX + UFH

**Percentage of patients**

Days since randomization

- TNK-TPA + UFH: 15.9%
- 1/2 TNK-TPA + abc + UFH: 6.5%
- 1/2 TNK-TPA + abc + ENOX: 3.5%
- TNK-TPA + ENOX: 4.4%

**Log rank**

P = 0.002

**Conclusions**

- Enoxaparin and UFH were equally effective in establishing early patency of the IRA.
- Enoxaparin was associated with a lower incidence of death/recurrent MI at 30 days.
- This advantage of enoxaparin was achieved with a similar risk of major hemorrhage.
- Half-dose TNK-TPA + abciximab appears to be associated with an increase in efficacy, but at the cost of an increase in major hemorrhage (vs. full-dose TNK-TPA).
**GUSTO V**

**30-day mortality**

![Graph showing 30-day mortality](image)

- OR = 0.95 [0.83 – 1.08]
- P = 0.45

**Endpoint:** 30-day mortality (n = 16,588)

- Reteplase (n = 8,260)
- Reteplase + abciximab (n = 8,328)

**Design**

- STEMI < 6 h
- rPA 10 + 10 U
- rPA 5 + 5 U abciximab

- 1st endpoint: 30-day mortality (n = 16,588)

**Reinfarction**

- Days from randomization
- Percentage of patients
- OR = 0.67 [0.55, 0.80]
- P < 0.0001

**Urgent PCI**

- Days from randomization
- Percentage of patients
- OR = 0.71 [0.65, 0.78]
- P < 0.0001

**Intracranial hemorrhage by age**

<table>
<thead>
<tr>
<th>Age ≤ 75</th>
<th>Age &gt; 75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reteplase</td>
<td>Reteplase + abciximab</td>
</tr>
<tr>
<td>2.03 (1.52, 2.71)</td>
<td>2.93 (1.52, 2.71)</td>
</tr>
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<table>
<thead>
<tr>
<th>Severe bleeding</th>
<th>Moderate bleeding</th>
<th>Transfusion (any)</th>
<th>RBC (any)</th>
<th>RBC (≥ 2 units)</th>
<th>Platelets</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>1.8</td>
<td>4.0</td>
<td>3.7</td>
<td>2.9</td>
<td>0.8</td>
</tr>
<tr>
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<td>3.5</td>
<td>5.7</td>
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**GUSTO V**

**Intracranial hemorrhage by age**

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</tr>
</tbody>
</table>

**GUSTO V**

**Bleeding complications**

<table>
<thead>
<tr>
<th>Bleeding complication</th>
<th>Reteplase (n = 8,260)</th>
<th>Reteplase + abciximab (n = 8,328)</th>
<th>OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe bleeding</td>
<td>0.5</td>
<td>1.1</td>
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</tbody>
</table>

**GUSTO V**

**Intracranial hemorrhage by age**

- OR 0.76
- P = 0.27

- OR 0.76
- P = 0.069
**Trials of IV GP IIb/IIIa antagonists and half-dose lytic**

- Marginal effect on early IRA patency
- Reduced incidence of ischemic complications such as reinfarction and refractory ischemia
- Less need for urgent PCI
- More ST segment resolution → better tissue perfusion?
- More non-cerebral bleeding complications especially in the elderly

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**Prehospital fibrinolysis: time saves lives**

- Meta analysis of large trials suggests 15-20% reduction in mortality with pre-hospital (vs. hospital based) lysis
- Benefit is maximized during first 2 hours (44% reduction).
- FFT estimate: benefit declines by 1.6 deaths prevented for 1000 patients treated, for every hour of delay.

---

**Lessons learned: the importance of time to treatment**

- Number of lives saved per 1000 patients treated with thrombolysis (based on 35-day mortality rates)
- Time from onset of symptoms to treatment:
  - 0-1: >1.0
  - 1-2: 0.75
  - 2-3: 0.5
  - 3-6: 0.25
  - >6: 0.1

---

**Pre hospital lysis**

- Meta analysis of large trials suggests 15-20% reduction in mortality with pre-hospital (vs. hospital based) lysis
- Benefit is maximized during first 2 hours (44% reduction).
- FFT estimate: benefit declines by 1.6 deaths prevented for 1000 patients treated, for every hour of delay.
Time to Balloon affects ST resolution

Pain to Balloon: Effect on 1 year mortality (Zwolle)

PCI VS. LYSIS: META – ANALYSIS OF 23 TRIALS

Meta-Analysis of 23 Randomized Trials of PCI vs Lysis (n=7739)
**ST- elevation MI**

Randomization

- Fibrinolysis
- PCI + stent (100 mg front loaded tPA)

---

**Registry data: fibrinolysis vs PCI**

- Door-to-needle: 42
- Door-to-balloon: 111
- In-hospital mortality
- 1-year mortality

---

**Referral hospitals**

Planned: 1,100 pts.

No transfer

Ambulance transfer

- Fibrinolysis (front loaded tPA)
- PCI

Incl. 1,129 pts.

**Angioplasty centers**

Planned: 800 pts.

- Fibrinolysis (front loaded tPA)
- PCI

Incl. 443 pts.

---

**DENMARK**

- 5.4 million inhabitants
- 5 PCI centers
- 24 referral hospitals
- 62% of Danish population
- Transport distance up to 95 US miles (mean 35 miles)

---

**Time from onset of symptoms to treatment (1,572 patients)**

<table>
<thead>
<tr>
<th>Hospitals</th>
<th>Fibrinolysis</th>
<th>PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Referral</td>
<td>Pre-hospital</td>
<td>Door-to-needle</td>
</tr>
<tr>
<td>Invasive</td>
<td>Prehospital</td>
<td>Door-to-needle</td>
</tr>
<tr>
<td>Referral</td>
<td>Pre-hospital</td>
<td>No-door-to-door</td>
</tr>
<tr>
<td>Invasive</td>
<td>Prehospital</td>
<td>Door-to-balloon</td>
</tr>
</tbody>
</table>

---

**Primary end point**

Death or reinfarction or disabling stroke within 30 days
Primary end points within 30 days
1,572 patients

- Death: 7.6%
p-value: 0.35

- Infarction: 6.6%
p-value: 0.0001

- Disabling stroke: 0.3%
p-value: 0.15

- Combined: 2.9%
p-value: 0.0003

Fibrinolysis vs PCI

NNT=15

Primary end point within 30 Days
1,572 patients

- Fibrinolysis (front-loaded tPA): 13.7%
  Log rank: p = 0.0003

- PCI: 8.0%

Primary end point: Death or reinfarction or stroke

Primary end point within 30 Days
Invasive centers: 443 patients

- Fibrinolysis (front-loaded tPA): 12.3%
  Log rank: p = 0.048

- PCI: 6.7%

Primary end point: Death or reinfarction or stroke

Primary end point within 30 Days
Referral hospitals: 1,129 patients

- Fibrinolysis (front-loaded tPA): 14.2%
  Log rank: p = 0.002

- PCI: 8.5%

Primary end point: Death or reinfarction or stroke

PRAGUE-2 Study aims:

- Thrombolysis or transport to PCI center for pts. with AMI presenting to small community hospitals without cath-lab?

- Mortality trial: Nationwide change of treatment guidelines for AMI in the Czech Republic?

Conclusion

An initial strategy of transferring pts. with ST - elevation MI for primary PCI is superior to accelerated tPA when transfer time is ≤ 3 hours.
**Treatment arms**

<table>
<thead>
<tr>
<th>Group TL (n=421)</th>
<th>Group PCI (n=429)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspegic 0.5 g</td>
<td>Aspegic 0.5 g</td>
</tr>
<tr>
<td>SK 1.5 mil. U</td>
<td>Heparin 200 U / kg</td>
</tr>
<tr>
<td>Treatment in the</td>
<td>Transport to PCI</td>
</tr>
<tr>
<td>community hospital</td>
<td>center</td>
</tr>
<tr>
<td>Ticlopidin 1 m.</td>
<td>Ticlopidin 1 m.</td>
</tr>
<tr>
<td>Fraxiparin 3 d.</td>
<td>Fraxiparin 3 d.</td>
</tr>
</tbody>
</table>

**30-day mortality (treatment used)**

<table>
<thead>
<tr>
<th>Group TL</th>
<th>Group PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.4</td>
<td>6.00</td>
</tr>
</tbody>
</table>

**30-day mortality (intention-to-treat)**

<table>
<thead>
<tr>
<th>Group TL</th>
<th>Group PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>7.1</td>
</tr>
</tbody>
</table>

**PRAGUE-2: Combined endpoint at 30 days (intention-to-treat)**

<table>
<thead>
<tr>
<th>Group TL</th>
<th>Group PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>15,2%</td>
<td>8,4%</td>
</tr>
</tbody>
</table>
**CAPTIM primary endpoint**

**CAPTIM: Time to Treatment and Mortality**

- **CAPTIM primary endpoint**
  - Time to treatment: 130 vs 190
  - n=840
  - 3R: 4.8
  - IPA: 3.7
  - PCI: 1.7
  - Combined: 0
  - 30 days: 8.2
  - 30 days: 9.2

**GRACIA - 2**

212 STEMI PATIENTS

- Primary PCI (stent, Reopro)
- TNK-tPA+ Enoxaparin
- PCI: 3-12h

**GRACIA - 2**

- TIMI 3 flow: 59% (lysis) vs. 14%
- ST resolution @ 6h: 61% in TNK arm, 43% in PCI arm
- LV function at 6 weeks, bleeding, MACE – similar
- Conclusion: If immediate PCI not available, lysis followed by systematic angiography & PCI offers similar results with similar safety

**GRACIA - 2**

- 212 STEMI patients randomized to:
  - TNK lysis alone -> rescue if needed
  - TNK lysis -> routine immediate angiography

**CAPTIM: comparison of angioplasty and prehospital thrombolysis in AMI**

1200 ST elevation AMI patients randomized, multicentered trial

- Primary angioplasty
- Prehospital fibrinolysis

- Composite endpoint: all-cause mortality, non-fatal recurrent MI, and non-fatal disabling stroke

**CAPITAL AMI**

- 170 high risk AMI patients randomized to:
  - TNK lysis alone -> rescue if needed
  - TNK lysis -> routine immediate angiography

**CAPTIM: Time to Treatment and Mortality**

- 170 high risk AMI patients randomized to:
  - TNK lysis alone -> rescue if needed
  - TNK lysis -> routine immediate angiography

- Primary PCI (stent, Reopro)
- TNK-tPA+ Enoxaparin
- PCI: 3-12h

**GRACIA - 2**

- TIMI 3 flow: 59% (lysis) vs. 14%
- ST resolution @ 6h: 61% in TNK arm, 43% in PCI arm
- LV function at 6 weeks, bleeding, MACE – similar
- Conclusion: If immediate PCI not available, lysis followed by systematic angiography & PCI offers similar results with similar safety
CONCLUSIONS

- When transport time does not exceed 60-90 minutes, and a competent team is on standby at the receiving hospital, transfer to PCI is superior to local lysis.
- Pre-hospital lysis is as good as primary PCI, provided “rescue” procedures are available.
- “drip & ship” - a valuable strategy
- Pre hospital “facilitation” - the best?

**Major efficacy results in CAPITAL-AMI**

<table>
<thead>
<tr>
<th>End point</th>
<th>Thrombolysis alone</th>
<th>Thrombolysis plus immediate transfer for angiography/PCI</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death/MI/stroke/recurrent ischemia (%)</td>
<td>21.4</td>
<td>9.3</td>
<td>Yes (p=0.034)</td>
</tr>
<tr>
<td>Death (%)</td>
<td>3.6</td>
<td>2.3</td>
<td>No</td>
</tr>
<tr>
<td>MI (%)</td>
<td>11.9</td>
<td>4.7</td>
<td>No</td>
</tr>
<tr>
<td>Stroke (%)</td>
<td>1.2</td>
<td>1.2</td>
<td>No</td>
</tr>
<tr>
<td>Recurrent ischemia (%)</td>
<td>17.9</td>
<td>7.0</td>
<td>Yes (p=0.037)</td>
</tr>
</tbody>
</table>

LeMay M. American College of Cardiology 2004 Scientific Sessions; Mar 7-10, 2004; New Orleans, LA.

**Plasminogen-Activator Angioplasty Compatibility Trial (PACT)**

Eligible acute infarct patients

**Patency of the Infarct Artery on Catheter Laboratory Arrival (Core Laboratory)**

Placebo vs t-PA

**CADILLAC Trial Design**

**Convalescent LV Function By Patency Group: Global Ejection Fraction**

### CADILLAC Trial Results

<table>
<thead>
<tr>
<th></th>
<th>PTCA (n=517)</th>
<th>PTCA + abciximab (n=528)</th>
<th>Stenting (n=511)</th>
<th>Stenting + abciximab (n=525)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIMI-3 flow</td>
<td>94%</td>
<td>92%</td>
<td>92%</td>
<td>96.7%</td>
</tr>
<tr>
<td>Recurrent Ischemia</td>
<td>4.5%</td>
<td>1.5%</td>
<td>3.9%</td>
<td>1.2%</td>
</tr>
<tr>
<td>Mortality</td>
<td>1.4%</td>
<td>1.0%</td>
<td>1.6%</td>
<td>1.6%</td>
</tr>
<tr>
<td>Need for Ischemic TVR</td>
<td>2.3%</td>
<td>0.2%</td>
<td>0.8%</td>
<td>0.2%</td>
</tr>
</tbody>
</table>

(1) 19.9% provisional stenting; (2) 15.0% provisional stenting; (3) about 5% crossover to abciximab

### ADMIRAL Study

**Design**
- AMI < 12 hours randomization
- Abciximab + Heparin, ASA, Ticlopidine
- Placebo + Heparin, ASA, Ticlopidine
- First Coronary Angiography
- PTCA + Stent
- Coronary Angiography at 24 h and 6 Months
- Clinical evaluation (24 h, 30 Days and 6 Months)

**Angiographic Results: TIMI 3 flow rates**

<table>
<thead>
<tr>
<th></th>
<th>% of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial</td>
<td>16.3%</td>
</tr>
<tr>
<td>After Balloon</td>
<td>83.7%</td>
</tr>
<tr>
<td>After stent</td>
<td>89.9%</td>
</tr>
<tr>
<td>24-hours</td>
<td>82.5%</td>
</tr>
</tbody>
</table>

**Primary Endpoint (30 days)**

- Death, Recurrent MI, Urgent TVR
- Placebo n = 150
- Abciximab n = 150

- Death: 15.3% Placebo vs. 7.3% Abciximab, p = 0.02
- Recurrent MI: 21.0% Placebo vs. 10.1% Abciximab
- Urgent TVR: 9.4% Placebo vs. 2.0% Abciximab
**ADMIRAL**

**Conclusions**

- In patients with acute myocardial infarction, abciximab in conjunction with primary stenting positively improved:
  - early TIMI 3 flow rate
  - left ventricular function
  - 30-day clinical results

- The excess in minor bleeding may be due to the 24-hour arterial sheath

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**Meta analysis of Reopro faciliation trials (Topol)**

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**On-TIME**

Ongoing-Tirofiban In Myocardial Infarction Evaluation

Flavio Ribichini, ESC 2003
Factors influencing choice of reperfusion strategy

- Risk of evolving MI
- Risk of bleeding
- Time required for performance of PCI by a skilled operator (local or elsewhere)
- Time from symptom onset

<table>
<thead>
<tr>
<th>Initial Flow</th>
<th>Early (n=243)</th>
<th>Late (n=244)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIMI 0</td>
<td>107 (44%)</td>
<td>143 (59%)</td>
<td>0.01</td>
</tr>
<tr>
<td>TIMI 1</td>
<td>32 (13%)</td>
<td>19 (8%)</td>
<td></td>
</tr>
<tr>
<td>TIMI 2</td>
<td>58 (24%)</td>
<td>46 (19%)</td>
<td></td>
</tr>
<tr>
<td>TIMI 3</td>
<td>46 (19%)</td>
<td>36 (15%)</td>
<td></td>
</tr>
<tr>
<td>TIMI 2 or 3</td>
<td>104 (43%)</td>
<td>82 (34%)</td>
<td>0.04</td>
</tr>
<tr>
<td>TIMI 3</td>
<td>46 (19%)</td>
<td>36 (15%)</td>
<td>0.22</td>
</tr>
</tbody>
</table>

PRINCIPLES OF REPERFUSION

- Hospitals should establish a system for administration of reperfusion therapy in the fastest possible way
- The MAXIMAL accepted times are 30 minutes for thrombolysis (Door to needle) and 90 minutes for PPCI (Door to balloon).
**THE APPROACH TO REPERFUSION THERAPY: II – Additional considerations**

- During first 3 hours no general preference of PCI over lysis
- Prefer PCI, even if somewhat delayed, if:
  - Shock or pulmonary edema
  - RV involvement
  - Contraindications to lysis
- Prefer lysis, if PCI available but delayed, during first 3 hours and if:
  - Time to balloon > 90 min
  - Time to balloon – time to needle >60min

**THE APPROACH TO REPERFUSION THERAPY: selecting mode of reperfusion**

- Class I ACC/AHA & ESC guidelines:
  - Primary PCI should be performed for AMI patients whenever it can be performed within 90 minutes of presentation by an experienced team
  - Thrombolysis should be given to STEMI patients presenting within 12 hours, for whom primary PCI is not available within 90 minutes, in the absence of C/I.

**GUIDELINES - BASED PHARMACOTHERAPY OF STEMI (2)**

<table>
<thead>
<tr>
<th>Disorder</th>
<th>ACC/AHA</th>
<th>ESC</th>
</tr>
</thead>
<tbody>
<tr>
<td>LMWH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>With lytics</td>
<td>IIb</td>
<td>Possible</td>
</tr>
<tr>
<td>With lytics, age &gt;75 or creat. &gt; 2.0</td>
<td>III</td>
<td></td>
</tr>
<tr>
<td>Anterior MI, large MI, AF</td>
<td>I</td>
<td></td>
</tr>
<tr>
<td>No reperfusion, no high risk</td>
<td>IIa, at least 48h</td>
<td></td>
</tr>
<tr>
<td>IIb/IIIa with PPCI</td>
<td>II</td>
<td>1 – POBA</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>II</td>
<td>Ia - stent</td>
</tr>
<tr>
<td>Post stenting</td>
<td>I</td>
<td></td>
</tr>
<tr>
<td>Alternative to ASA post lysis</td>
<td>IIa</td>
<td>No data</td>
</tr>
</tbody>
</table>

**GUIDELINES - BASED PHARMACOTHERAPY OF STEMI (1)**

<table>
<thead>
<tr>
<th>Disorder</th>
<th>ACC/AHA</th>
<th>ESC</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA</td>
<td>Class I for all, starting on presentation, indefinitely</td>
<td></td>
</tr>
<tr>
<td>UFH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>With primary PCI</td>
<td>I</td>
<td></td>
</tr>
<tr>
<td>With t-PA &amp; variants</td>
<td>I</td>
<td></td>
</tr>
<tr>
<td>With SK if ant. MI, large MI, AF</td>
<td>I</td>
<td></td>
</tr>
<tr>
<td>Other SK</td>
<td>IIb</td>
<td>IIa</td>
</tr>
<tr>
<td>No reperfusion</td>
<td>IIa, at least 48h</td>
<td></td>
</tr>
</tbody>
</table>

**THE APPROACH TO REPERFUSION THERAPY: II – Hospital phase**

- PCI available locally within 90 min.
- PCI available elsewhere within 90 min
- Transfer, Consider facilitation (t-PA, Reopro)
- PCI unavailable within 90-120 min.
- Lysis

- As needed
<table>
<thead>
<tr>
<th>GUIDELINES - BASED PHARMACOTHERAPY OF STEMI (3)</th>
<th>GUIDELINES - BASED PHARMACOTHERAPY OF STEMI (4)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STATINS</strong></td>
<td><strong>ACC/AHA</strong></td>
</tr>
<tr>
<td>Any LDL</td>
<td>I</td>
</tr>
<tr>
<td>LDL &gt; 115 despite diet</td>
<td>I</td>
</tr>
<tr>
<td><strong>FIBRATE/NIACIN</strong></td>
<td><strong>ACC/AHA</strong></td>
</tr>
<tr>
<td>LDL&lt;100+ HDL &lt;40 or TG&gt;500</td>
<td>I</td>
</tr>
<tr>
<td>I if HDL &lt;45 + TG&gt;200</td>
<td>I</td>
</tr>
<tr>
<td><strong>WARFARIN</strong></td>
<td><strong>ACC/AHA</strong></td>
</tr>
<tr>
<td>ASA allergy, AF, LV clot</td>
<td>I</td>
</tr>
<tr>
<td>With ASA if &lt;75</td>
<td>Ia</td>
</tr>
</tbody>
</table>

**β blockers**
- Early IV
- Hospital phase
- Long term, low risk
- Verapamil/diltiazem if β blockers not tolerated
- With LV dysfunction
- 1st 24h, low risk

**WARFARIN**
- ASA allergy, AF, LV clot
- With ASA if <75

**ACE-I**
- I