Chest pain in the night ......

ACCA 2017 London
P Goldstein
Lille university hospital
Patrick GOLDSTEIN
Conflicts of interest

Speakers and Consultant

boehringer Ingelheim
astra zeneca,
Receiving the call

A true medical decision
Mr S., 54 years old, call our SAMU at 3H30
Since 2:30 am, he has been suffering from chest pain
He was awakened by this dolor
He feels something like a dyspnea
The pain is nitrate-resistant (patient has his own medication)
What are the first criteria needed in the dispatching centre for a correct emergency decision?
Call to a dispatch center

Numerous media campaigns since the early 2000s, supported by regional and national health authorities
Impact of media campaigns on time to first call in STEMI patients
France 2000-2010

<table>
<thead>
<tr>
<th></th>
<th>2000</th>
<th>2005</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median time from</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>onset to 1st call (min)</td>
<td>120 [41; 360]</td>
<td>90 [30; 295]</td>
<td>74 [30; 240]</td>
</tr>
</tbody>
</table>

EMS (SAMU) as 1st intervening party

<table>
<thead>
<tr>
<th></th>
<th>2000</th>
<th>2005</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>23,2</td>
<td>41,3</td>
<td>48,8</td>
</tr>
</tbody>
</table>
M.I.C.U.
ARRIVAL MICU 3:50 am
EVALUATION:

1. Evaluate breathing; is he able to speak?
   - Life emergency?

2. Characteristics of the pain

3. Research history of CVD or a family history

4. Current treatment

5. Hyperthermia
• **History:** unstable angina, pulmonary oedema

• **Risks factors:** hypertension, hypercholesterolaemia, moderately overweight, diabetes, current smoker

• **TT:** molsidomine, furosemide, ramipril metoprolol, glimepiridine, insulin NPH profile 40

• Patient treated by a cardiologist

• **Now, what decision for this patient**
### Important delays and treatment goals in the management of acute STEMI

<table>
<thead>
<tr>
<th>Delay</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred for FMC to ECG and diagnosis</td>
<td>(\leq 10) min</td>
</tr>
<tr>
<td>Preferred for FMC to fibrinolysis (‘FMC to needle’)</td>
<td>(\leq 30) min</td>
</tr>
<tr>
<td>Preferred for FMC to primary PCI (‘door to balloon’) in primary PCI hospitals</td>
<td>(\leq 60) min</td>
</tr>
</tbody>
</table>
| Preferred for FMC to primary PCI                                     | \(\leq 90\) min  
  (\(\leq 60\) min if early presenter with large area at risk) |
| Acceptable for primary PCI rather than fibrinolysis                 | \(\leq 120\) min 
  (\(\leq 90\) min if early presenter with large area at risk)  
  if this target cannot be met, consider fibrinolysis. |
| Preferred for successful fibrinolysis to angiography                | 3–24 h |

FMC = first medical contact; PCI = percutaneous coronary coronary intervention.
MICU: 4.00 am

- AP: 200/90 mmHg - R, 190/92 mmHg - L
- HR: 55/min
- Killip 1
- $\text{SpO}_2$: 93%
- Glycaemia: 1.7g/l
- Pain estimate: 70/100
- ECG 18 leads and compared to previous
STEMI diagnosis: Triage on scene

- General organisation
  - Chest pain characteristics
  - Clinical examination

ECG – 12 or 18 leads

- Analysis of ECG
- Clinical check list
- No medical validation
  +/-

- Clinical examination
- Analysis by the internal software
  +

- Medical validation
  +++

Physicians on board or
Teletransmission to cardiology center

Courtesy P. Goldstein
Pre-hospital diagnosis of AMI – Tele-ECG

MD ambulance

12-lead ECG
LIFEPAK 12
Medtronic

GSM

CCU

Attending cardiologist

ER
• The doctor must be available 24 h / 24 h for analysis and validation online

• Transmission must not be an indirect factor prolonging the delay to reperfusion
Management of AMI in the field or ED

Diagnostic criteria

Typical (80%)

- Typical chest pain
- ECG: ST elevation >1 mm in 2 or more limb leads or >2 mm in 2 or more chest leads
- Non-relief of pain and ECG alterations by sublingual nitrates

Atypical (20%)

- Atypical pain
- ECG: ST depression, non Q-waves or quite normal, LBBB ...
  ⇒ Unstable angina or AMI, pericarditis...
  ⇒ Medical transportation
  ⇒ CPK, echocardio, angiography
Biomarkers in pre H setting?
Here is the ECG
It’s an acute extensive anterior myocardial infarction
You are close to the nearest cath lab
less than 90 minutes

Strategy?
Prehospital and in-hospital management, and reperfusion strategies within 24 h of FMC

STEMI diagnosis*

Primary-PCI capable center

Preferably <60 min

Primary-PCI

Rescue PCI

Immediately

No

Preferably 3–24 h

Coronary angiography

EMS or non primary-PCI capable center

PCI possible <120 min?

Yes

Immediate transfer to PCI center

Preferably ≤90 min
(≤60 min in early presenters)

Successful fibrinolysis?

Immediate transfer to PCI center

Immediate fibrinolysis

No

Preferably ≤30 min

*The time point the diagnosis is confirmed with patient history and ECG ideally within 10 min from the first medical contact (FMC). All delays are related to FMC (first medical contact).

Cath = catheterization laboratory; EMS = emergency medical system; FMC = first medical contact; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.
Following the guidelines

• Go to CATH

• But
  – Focus on DAP and asap DAP
  – Anti thrombin therapy
  – Pain treatment and some more little things …
UNE SAIGNÉE!
TROPOinine!
VENTOUSES!
ECG!
COURBE DE TEMPERATURE!
DES SANGSUES QUE DIABLE!

PAS DU TOUT
VUE SES URINES

PITIE! APPELEZ MON CARDIOLOGUE!

CHAVINU
AAP ?
Study population and design

- Documented evidence of STEMI
- Planned for angioplasty (PCI)

- Onset of ischaemic symptoms within 6 h
- Initially managed by ambulance physician/personnel; also concerning patients not pre-treated for STEMI in emergency rooms of non-PCI hospitals

STE-ACS planned for PCI (N = 1862)

Randomised, double-blind

- Ticagrelor 180 mg loading dose
- Pre-hospital
- Placebo loading dose
- In-Hospital
- Ticagrelor 180 mg loading dose

≥ 70% ST-segment elevation resolution pre-PCI

Primary Objectives

OR

TIMI flow grade 3 of MI culprit vessel at initial angiography

Ticagrelor 90 mg/bid 30 days

Median times to pre- and in-hospital steps

Onset of Symptoms → EKG Pre-hospital → LD1 → Randomization → LD2 → EKG Pre-PCI → Angiography → PCI

- 73 min
- 31 min
- 14 min

- 90 min
- 63 min
- 28 min

- 159 min
1st Co-primary endpoint
No ST-segment resolution (≥70%)

Primary objective

\[ p = \text{NS} \]

<table>
<thead>
<tr>
<th></th>
<th>Pre-hospital</th>
<th>In-hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-PCI</td>
<td>86.8%</td>
<td>87.6%</td>
</tr>
<tr>
<td>Post-PCI 1 hour after PCI</td>
<td>42.5%</td>
<td>47.5%</td>
</tr>
</tbody>
</table>

\[ p = 0.055 \text{ (NS)} \]
### Absence of ST-segment resolution by patient characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Odds ratio (95% CI)</th>
<th>Total patients</th>
<th>Endpoint rate</th>
<th>OR (95% CI)</th>
<th>P Value (int.)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 years</td>
<td></td>
<td>1014</td>
<td>85.9%</td>
<td>87.3%</td>
<td>0.887 (0.618, 1.272)</td>
</tr>
<tr>
<td>≥65 years</td>
<td>584</td>
<td>88.6%</td>
<td>88.2%</td>
<td>1.037 (0.625, 1.724)</td>
<td>0.2940</td>
</tr>
<tr>
<td>&lt;75 years</td>
<td>1348</td>
<td>86.7%</td>
<td>86.8%</td>
<td>0.994 (0.726, 1.362)</td>
<td>0.2940</td>
</tr>
<tr>
<td>≥75 years</td>
<td>250</td>
<td>87.6%</td>
<td>92.0%</td>
<td>0.617 (0.269, 1.418)</td>
<td>0.2940</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1288</td>
<td>87.0%</td>
<td>87.7%</td>
<td>0.945 (0.680, 1.312)</td>
<td>0.8292</td>
</tr>
<tr>
<td>Female</td>
<td>310</td>
<td>85.9%</td>
<td>87.5%</td>
<td>0.871 (0.451, 1.684)</td>
<td>0.8292</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>212</td>
<td>88.3%</td>
<td>88.1%</td>
<td>1.015 (0.438, 2.353)</td>
<td>0.8319</td>
</tr>
<tr>
<td>No</td>
<td>1386</td>
<td>86.6%</td>
<td>87.5%</td>
<td>0.922 (0.673, 1.261)</td>
<td>0.8319</td>
</tr>
<tr>
<td><strong>Location of MI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>831</td>
<td>89.0%</td>
<td>87.3%</td>
<td>1.183 (0.775, 1.808)</td>
<td>0.1320</td>
</tr>
<tr>
<td>Non-anterior</td>
<td>767</td>
<td>84.7%</td>
<td>88.0%</td>
<td>0.750 (0.495, 1.136)</td>
<td>0.1320</td>
</tr>
<tr>
<td><strong>TIMI risk score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–2</td>
<td>971</td>
<td>86.0%</td>
<td>87.6%</td>
<td>0.867 (0.597, 1.256)</td>
<td>0.7129</td>
</tr>
<tr>
<td>3–6</td>
<td>599</td>
<td>88.3%</td>
<td>87.4%</td>
<td>1.081 (0.661, 1.767)</td>
<td>0.7129</td>
</tr>
<tr>
<td>&gt;6</td>
<td>28</td>
<td>86.7%</td>
<td>92.3%</td>
<td>0.542 (0.043, 6.757)</td>
<td>0.7129</td>
</tr>
<tr>
<td><strong>Highest Killip Classification pre-PCI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>1458</td>
<td>86.1%</td>
<td>88.2%</td>
<td>0.833 (0.612, 1.133)</td>
<td>0.1049</td>
</tr>
<tr>
<td>&gt;I</td>
<td>82</td>
<td>93.5%</td>
<td>83.3%</td>
<td>2.865 (0.664, 12.236)</td>
<td>0.3455</td>
</tr>
<tr>
<td><strong>Prior ASA use</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>476</td>
<td>88.8%</td>
<td>87.1%</td>
<td>1.178 (0.670, 2.075)</td>
<td>0.3455</td>
</tr>
<tr>
<td>No</td>
<td>1122</td>
<td>86.1%</td>
<td>87.9%</td>
<td>0.856 (0.604, 1.214)</td>
<td>0.3455</td>
</tr>
<tr>
<td><strong>GPIIb/IIIa inhibitor use before angiography</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>117</td>
<td>85.2%</td>
<td>83.9%</td>
<td>1.106 (0.405, 3.021)</td>
<td>0.7281</td>
</tr>
<tr>
<td>No</td>
<td>1481</td>
<td>87.0%</td>
<td>87.9%</td>
<td>0.918 (0.675, 1.248)</td>
<td>0.7281</td>
</tr>
<tr>
<td><strong>Morphine use for index event/PCI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>800</td>
<td>90.8%</td>
<td>86.8%</td>
<td>1.493 (0.954, 2.331)</td>
<td>0.0050</td>
</tr>
<tr>
<td>No</td>
<td>798</td>
<td>82.8%</td>
<td>88.4%</td>
<td>0.632 (0.423, 0.943)</td>
<td>0.0050</td>
</tr>
</tbody>
</table>

Pre-hospital better ← 0.5 → 1 → 2 → In-hospital better
Definite stent thrombosis up to 30 days

Ticagrelor pre-hospital 2/906 (0.2%) versus Ticagrelor in-hospital 11/952 (1.2%)
OR 0.19 (95% CI 0.04, 0.86), P=0.0225
Hypothesis of the present analysis

- It was hypothesized that the effect of earlier, pre-hospital ticagrelor may not have manifested until after PCI

ECG, electrocardiogram; LD, loading dose.

## Post-PCI coronary reperfusion

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Pre-hospital ticagrelor</th>
<th>In-hospital ticagrelor</th>
<th>Odds ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TIMI flow grade 3 of MI culprit vessel post-PCI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of subjects&lt;sup&gt;a&lt;/sup&gt;</td>
<td>760</td>
<td>784</td>
<td>1.132 (0.876–1.462)</td>
<td>0.34</td>
</tr>
<tr>
<td>n (%)</td>
<td>625 (82.2)</td>
<td>630 (80.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ST-segment elevation resolution ≥70% post-PCI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of subjects&lt;sup&gt;a&lt;/sup&gt;</td>
<td>713</td>
<td>743</td>
<td>1.225 (0.996–1.506)</td>
<td>0.054</td>
</tr>
<tr>
<td>n (%)</td>
<td>410 (57.5)</td>
<td>390 (52.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Degree of ST-segment elevation resolution post-PCI (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of subjects&lt;sup&gt;a&lt;/sup&gt;</td>
<td>713</td>
<td>743</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>66.7 (36.8)</td>
<td>63.9 (34.3)</td>
<td>–</td>
<td>0.049&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Median</td>
<td>75.0</td>
<td>71.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>Subjects with a PCI performed for the index event and available data on TIMI flow or ST-segment elevation.

<sup>b</sup>p-value from non-parametric Wilcoxon test, comparing median degree of resolution.
• Pre-hospital ticagrelor effect on platelet function appears after PCI
• Largest between-group difference observed 1–6 h after PCI

Values are median (IQR); MD, maintenance dose
p-values were all NS
Factors associated with infarct-related artery patency before primary PCI for STEMI

Results from the FAST-MI 2010 registry

E. Puymirat¹, P. Coste², S. Cattan³, D. Blanchard⁴, C. Brasselet⁵, M. Elbaz⁶, PG. Steg⁷, F. Schiele⁸, T. Simon⁹, N. Danchin¹

IRA patency and pre-hospital antiplatelet agents according to time delays and PH morphine use

Onset to call <75
Onset to call ≥75

None/ASA alone
Clopidogrel
Prasugrel
GP IIb-IIIa

ECG to angio <90
ECG to angio ≥90

None/ASA alone
Clopidogrel
Prasugrel
GP IIb-IIIa

PH prasugrel
No PH prasugrel

No morphine
Morphine

PH GPI
No PH GPI

None/ASA alone
Clopidogrel
Prasugrel
GP IIb-IIIa
IRA patency according to time and pre-hospital anticoagulant agents

Onset to call <75
Onset to call ≥75

ECG to angio <90
ECG to angio ≥90

None
UFH
LMWH, fond, biva
### Independent correlates of IRA patency

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom onset to call &lt; 75 min</td>
<td>1.60 (1.26-2.03)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ECG to angio &gt; 90 min</td>
<td>1.38 (1.08-1.77)</td>
<td>0.009</td>
</tr>
<tr>
<td>Pre-hospital</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- clopidogrel</td>
<td>1.19 (0.91-1.56)</td>
<td>0.20</td>
</tr>
<tr>
<td>- prasugrel</td>
<td>1.80 (1.19-2.72)</td>
<td>0.005</td>
</tr>
<tr>
<td>Admission SBP (per mm Hg)</td>
<td>1.005 (1.001-1.010)</td>
<td>0.01</td>
</tr>
<tr>
<td>Pre-hospital morphine</td>
<td>0.69 (0.50-0.95)</td>
<td>0.02</td>
</tr>
</tbody>
</table>
In-hospital complications in relation with use and timing of pre-hospital antithrombotic medications in STEMI patients.

The FAST-MI 2010 registry


Hospital Regional University of Lille, Department of Emergency, Lille, France, University Hospital of Toulouse-Rangueil, France, University Hospital of Bocage, Dijon, France, University Hospital of Clermont-Ferrand, France, University Hospital of Rennes -Pontchaillou, France, Hospital of La Rochelle, France, University Hospital of Nantes, France, AP-HP - Hospital Saint-Antoine, Paris, France, AP-HP - European Hospital Georges Pompidou, Paris, France
Thirty-day mortality according to time from onset to call

- Time ≤ 60 min: 3.2
- Time > 60 min: 3.3
Prehospital medications are correlated with survival in patients seen early.

Time onset to call ≤ 60 minutes

Time onset to call > 60 minutes

***: P <0.001
Prehospital anticoagulants

Time onset to call ≤ 60 minutes

No heparin: 6.4
UFH: 1.9
Enoxaparin: 0.8
Heparins: 1.4

Time onset to call > 60 minutes

No heparin: 4
UFH: 2.8
Enoxaparin: 2
Heparins: 2.6

***: P <0.001
Prehospital antiplatelet agents

Time onset to call ≤ 60 minutes

<table>
<thead>
<tr>
<th></th>
<th>No antiplatelet</th>
<th>Aspirin alone</th>
<th>Clopidogrel</th>
<th>Prasugrel</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>P = 0.001</strong></td>
<td>6,7</td>
<td>6,1</td>
<td><strong>1,9</strong></td>
<td><strong>0</strong></td>
</tr>
</tbody>
</table>

Time onset to call > 60 minutes

<table>
<thead>
<tr>
<th></th>
<th>No antiplatelet</th>
<th>Aspirin alone</th>
<th>Clopidogrel</th>
<th>Prasugrel</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>P = 0.001</strong></td>
<td>3,8</td>
<td>6,1</td>
<td>2,8</td>
<td>1,4</td>
</tr>
</tbody>
</table>
This extremely rapid access to PCI in ATLANTIC contrasts with real-life observations: in patients following an optimal pathway in the French Registry of Acute ST-Elevation and Non-ST-Elevation Myocardial Infarction 2010 registry, time from symptom onset to PCI was still 43 minutes longer than what was observed in the ATLANTIC trial. In this registry, prehospital administration of prasugrel in patients with STEMI treated with primary PCI was associated with a higher likelihood of infarct-related artery patency, defined as TIMI 2 or 3 flow before the procedure. Such observational data suggest that administration of a potent P2Y12 inhibitor before coronary angiography may improve early infarct-related artery patency when time delays are longer than what was observed in the ATLANTIC trial.

In conclusion, further studies are needed to determine the clinical impact of pretreatment with DAPT in the setting of ACS. Meanwhile, early administration of DAPT seems to be a reasonable therapeutic strategy in daily clinical practice.

L De Luca, N Danchin, M Valgimini, P Goldstein
Am J Cardiology 2015;116:660-668
Anti GP 2B3A
Acute myocardial infarction diagnosed in ambulance or referral center
ASA + 600 mg Clopidogrel + UFH

ON-TIME -2

N=984

Placebo

Tirofiban *

Transportation

PCI center

Angiogram

Tirofiban provisional

PCI

Angiogram

Tirofiban cont’d

*Bolus: 25 µg/kg & 0.15 µg/kg/min infusion
ADMIRAL6-month primary EP

-89%

-31%

-53%
Antithrombic therapy before, during and after emergency angioplasty for STEMI patients
S Savonitto, Giuseppe De Luca, P Goldstein
European Heart Journal ACCare, 2015 1-18
The effect of cangrelor versus clopidogrel on periprocedural outcomes in a pooled analysis of patient-level data

Christian W. Hamm

for the CHAMPION Executive Committees and Investigators
ANTICOAGULATION ?????
ATOLL
An international randomized study comparing IV enoxaparin to IV UFH in primary PCI


**ATOLL**: Acute STEMI Treated with primary PCI and intravenous enoxaparin Or UFH to Lower ischemic and bleeding events at short- and Long-term follow-up (Investigator-driven study)

**G. Montalescot, Disclosure**: Research Grants (to the Institution) from Abbott Vascular, Bristol Myers Squibb, Boston Scientific, Centocor, Cordis, Eli-Lilly, Fédération Française de Cardiologie, Fondation de France, Guerbet Medical, INSERM, Medtronic, Pfizer, Sanofi-Aventis Group, Société Française de Cardiologie; Consulting or Lecture Fees from Accumetrics, Astra-Zeneca, Bayer, Biotronik, Boehringer-Ingelheim, Bristol-Myers Squibb, Daichi-Sankyo, Eisai, Eli-Lilly, Menarini, MSD, Novartis, Pfizer, Portola, Sanofi-Aventis Group, Schering-Plough, Servier and The Medicines Company.
**ATOLL Trial design**

Randomization as *early* as possible (MICU ++++)

*Real life* population (shock, cardiac arrest included)

*No anticoagulation* and no lytic *before* Rx

*Similar antiplatelet* therapy in both groups

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**STEMI → Primary PCI**

**ENOXAPARIN IV**

0.5 mg/kg

with or without GPIIbIIIa

**UFH IV**

50-70 IU with GP IIbIIIa

70-100 IU without GP IIbIIIa

(Dose ACT-adjusted)

**IVRS**

**Primary PCI**

**ENOXAPARIN SC**

**UFH IV or SC**

---

**30 days**

1° EP: Death, Complication of MI, Procedure Failure, Major Bleeding

Main 2° EP: Death, recurrent MI/ACS, Urgent Revascularization
Primary Endpoint
Death, Complication of MI, Procedure Failure or Major Bleeding

% of patients

RRR = 17%
P = 0.07

33.7
28

UFH
ENOX
Main Secondary Endpoint

Death, Recurrent MI/ACS or Urgent Revascularization

RRR = 41%
P = 0.016

% of patients

UFH
ENOX
Results of the EUROMAX trial

Philippe Gabriel Steg*, Arnoud van ‘t Hof, Christian W. Hamm, Peter Clemmensen, Frédéric Lapostolle, Pierre Coste, Jurrien Ten Berg, Pierre Van Grunsven, Gerrit Jan Eggink, Lutz Nibbe, Uwe Zeymer, Marco Campo dell' Orto, Holger Nef, Jacob Steinmetz, Louis Soulat, Kurt Huber, Efthymios N. Deliargyris, Debra Bernstein, Diana Schuette, Jayne Prats, Tim Clayton, Stuart Pocock, Martial Hamon, Patrick Goldstein, for the EUROMAX Investigators**

*
## Outcomes, 30 days, con’t

<table>
<thead>
<tr>
<th></th>
<th>Bivalirudin (N=1089)</th>
<th>Heparins with optional GPI (N=1109)</th>
<th>Relative risk [95% CI]</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reinfarction</strong></td>
<td>19 (1.7)</td>
<td>10 (0.9)</td>
<td>1.93 (0.90–4.14)</td>
<td>0.08</td>
</tr>
<tr>
<td><strong>Q-wave</strong></td>
<td>3 (0.3)</td>
<td>2 (0.2)</td>
<td>1.53 (0.26–9.12)</td>
<td>0.68</td>
</tr>
<tr>
<td><strong>Non-Q-wave</strong></td>
<td>16 (1.5)</td>
<td>8 (0.7)</td>
<td>2.04 (0.88–4.74)</td>
<td>0.09</td>
</tr>
<tr>
<td><strong>Stent thrombosis (ARC definition(^9))</strong></td>
<td>17 (1.6)</td>
<td>6 (0.5)</td>
<td><strong>2.89 (1.14–7.29)</strong></td>
<td><strong>0.02</strong></td>
</tr>
<tr>
<td><strong>Definite</strong></td>
<td>17 (1.6)</td>
<td>6 (0.5)</td>
<td><strong>2.89 (1.14–7.29)</strong></td>
<td><strong>0.02</strong></td>
</tr>
<tr>
<td><strong>Probable</strong></td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>–</td>
<td>n/a</td>
</tr>
<tr>
<td><strong>Acute (≤24 hours)</strong></td>
<td>12 (1.1)</td>
<td>2 (0.2)</td>
<td><strong>6.11 (1.37, 27.24)</strong></td>
<td><strong>0.007</strong></td>
</tr>
<tr>
<td><strong>Subacute (&gt;24 hours to 30 days)</strong></td>
<td>5 (0.5)</td>
<td>4 (0.4)</td>
<td>1.27 (0.34–4.73)</td>
<td>0.75</td>
</tr>
<tr>
<td><strong>Ischemia-driven revascularization</strong></td>
<td>24 (2.2)</td>
<td>17 (1.5)</td>
<td>1.44 (0.78–2.66)</td>
<td>0.25</td>
</tr>
<tr>
<td><strong>Reinfarction, ischemia-driven revascularization or stent thrombosis</strong></td>
<td>29 (2.7)</td>
<td>21 (1.9)</td>
<td>1.41 (0.81–2.45)</td>
<td>0.23</td>
</tr>
<tr>
<td><strong>Any stroke(^*)</strong></td>
<td>6 (0.6)</td>
<td>11 (1.0)</td>
<td>0.56 (0.21–1.50)</td>
<td>0.24</td>
</tr>
<tr>
<td><strong>Ischemic</strong></td>
<td>6 (0.6)</td>
<td>9 (0.8)</td>
<td>0.68 (0.24–1.9)</td>
<td>0.46</td>
</tr>
<tr>
<td><strong>Hemorrhagic</strong></td>
<td>0</td>
<td>2 (0.2)</td>
<td>Not applicable</td>
<td>0.50</td>
</tr>
<tr>
<td><strong>Acquired thrombocytopenia</strong></td>
<td>7 (0.7)</td>
<td>14 (1.4)</td>
<td>0.50 (0.20–1.24)</td>
<td>0.13</td>
</tr>
</tbody>
</table>

n/a: not applicable.
Determinants of prehospital use of opioids in AMI patients and association with early outcomes.

The FAST-MI 2010 registry

N. Bonnet¹, A. Lafont¹, N. Danchin¹, L. Lamhaut², L. Mock³, N. Dos Santos Teixeira¹, P. Goldstein⁴, F. Schiele⁵, T. Simon⁶, E. Puymirat¹

(1) Hôpital Européen Georges Pompidou, Paris, (2) SAMU de Paris, (3) Clinique de Fontaine, Fontaine-lès-Dijon, (4) SAMU de Lille, (5) Hôpital Jean Minjoz, Besançon, (6) CHU St Antoine, Paris, France
### Independent correlates of pre-hospital use of morphine

<table>
<thead>
<tr>
<th>Factor</th>
<th>Adjusted OR (95%CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; 60 years</td>
<td>2.82 (1.78-4.46)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>STEMI (vs NSTEMI)</td>
<td>4.66 (3.32-6.53)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chest pain score ≥ 7</td>
<td>2.88 (2.00-4.14)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Typical chest pain</td>
<td>2.17 (1.37-3.45)</td>
<td>0.001</td>
</tr>
<tr>
<td>Female sex</td>
<td>0.74 (0.54-1.02)</td>
<td>0.06</td>
</tr>
</tbody>
</table>
### Hemodynamic correlates of morphine use

<table>
<thead>
<tr>
<th></th>
<th>No P-H morphine</th>
<th>P-H morphine</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial heart rate (bpm)</td>
<td>80.6 ± 21.2</td>
<td>74.5 ± 19.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Initial SBP (mm Hg)</td>
<td>147.3 ± 29.3</td>
<td>140.0 ± 28.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Change in HR</td>
<td>+ 4.3 ± 19.6</td>
<td>- 1.9 ± 19.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Change in SBP</td>
<td>10.5 ± 28.6</td>
<td>13.7 ± 28.0</td>
<td>0.06</td>
</tr>
<tr>
<td>Change in Killip class</td>
<td>0.077 ± 0.355</td>
<td>0.080 ± 0.366</td>
<td>0.87</td>
</tr>
</tbody>
</table>
Results: in-hospital complications

<table>
<thead>
<tr>
<th>Event</th>
<th>No morphine</th>
<th>Morphine</th>
<th>Adjusted OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent ischemia</td>
<td>4</td>
<td>2.2</td>
<td>0.70 (0.33-1.49)</td>
</tr>
<tr>
<td>Re-MI</td>
<td>1</td>
<td>2</td>
<td>2.53 (1.01-6.33)</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>1</td>
<td>0.7</td>
<td>1.26 (0.27-5.97)</td>
</tr>
<tr>
<td>Death</td>
<td>1</td>
<td>1</td>
<td>1.32 (0.46-3.82)</td>
</tr>
<tr>
<td>Major bleed</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Transfusion</td>
<td>3</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>3</td>
<td>1.5</td>
<td></td>
</tr>
</tbody>
</table>
One-year survival

Adjusted HR (95%CI)

- Model 1
  0.46 (0.25-0.83), P=0.01

- Model 2
  0.53 (0.29-0.97), P=0.04

Adjusted for
- Model 1: GRACE score
- Model 2: age, sex, region, type of centre, clinical profile, medical history, GRACE score, early in-hospital medications, PCI

Pre-hospital morphine
No pre-hospital morphine

% survival

0  3  6  9  12
Months
Morphine delays and attenuates ticagrelor exposure and action in patients with myocardial infarction: the randomized, double-blind, placebo-controlled IMPRESSION trial

Patients initially assessed as eligible (n = 74)

Randomized (n = 74)

Allocated to morphine (n = 37)

Allocated to placebo (n = 37)

5 mg

Excluded from the primary analysis (n = 2), reasons:
- required morphine due to chest pain aggravation (n = 1)
- initial diagnosis of STEMI not confirmed (n = 1)

Completed PK and PD assessment (n = 35)

Excluded from the primary analysis (n = 2), reasons:
- required morphine due to chest pain aggravation (n = 2)

Completed PK and PD assessment (n = 35)

Ticagrelor 180 mg
Réduction de l’exposition de 36% du ticagrelor et de son métabolite actif. Augmentation du délai d’obtention d’une concentration maximale (4H vs 2h)
CRUSH study


The effect of crushing prasugrel on pharmacokinetic and pharmacodynamic profiles. STEMI = ST-segment elevation myocardial infarction.

Platelet reactivity was assessed at baseline, 1, 2, 4, and 8 h after a 180-mg ticagrelor loading dose in patients treated by crushed tablets (diamonds) or integral tablets (squares). Data are expressed as mean ± SD.
OXYGEN «The first cause of surprise is …..the extraordinary paucity of scientific data on one of its (myocardial infarction) most widely used methods of treatment. The second disturbing finding is that oxygen therapy, far from having been proved to be efficacious, might even be deleterious… »

Systematic review (2009) Only 2 randomized clinical trials, N< 250 patients

Results in the largest trial, N~200 (1976):

<table>
<thead>
<tr>
<th></th>
<th>Oxygen</th>
<th>Air</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>11.3%</td>
<td>3.9%</td>
<td>0.08</td>
</tr>
<tr>
<td>ASAT* (mean)</td>
<td>99.9 IU/ml</td>
<td>80.7 IU/ml</td>
<td>0.05</td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td>13.8%</td>
<td>6.5%</td>
<td>0.13</td>
</tr>
</tbody>
</table>

*Used as a surrogate for infarct size

2 Wijesinghe M et al Heart 2009;95:198–202
You are far away from the nearest cathlab - more than 90 minutes after this ECG.

What is your therapeutic strategy?
Prehospital and in-hospital management, and reperfusion strategies within 24 h of FMC

STEMI diagnosis

Primary-PCI capable center
- Preferably <60 min
  - Primary-PCI
  - Rescue PCI
    - Immediately
      - No
      - Yes
    - Preferably 3–24 h
      - Coronary angiography

EMS or non primary-PCI capable center
- PCI possible <120 min?
  - Yes
    - Immediate transfer to PCI center
    - Preferably ≤90 min (≤60 min in early presenters)
  - No
    - Preferably ≤30 min
      - Immediate fibrinolysis

*The time point the diagnosis is confirmed with patient history and ECG ideally within 10 min from the first medical contact (FMC).
All delays are related to FMC (first medical contact).
What kind of medication you start with?

- **Heparin**: 60 IU/kg bolus i.v. (max 4,000 IU) followed by 12 IU/kg/h (max 1,000 IU/h) or enoxaparin (Extract)

- **Aspirin**: 250 mg i.v.

- **Clopidogrel**: loading dose of 300 mg

---

Extract-TIMI 25: World Congress of Cardiology - Barcelona 2006
Enoxaparin results in less death than unfractionated heparin
10.7 vs 13.8 (p=0.001) (M GIBSON, USA)
CLARITY ambulance substudy: pre-hospital clopidogrel vs. placebo (plus fibrinolytic therapy)

- 3,491 patients aged <76 years with STEMI, receiving fibrinolytic therapy
- Randomised to clopidogrel or placebo in the ambulance or on admission

Clopidogrel given in the ambulance is associated with ST-segment resolution

P2Y12 receptor inhibitor with prasugrel and ticagrelor in STEMI patients after fibrinolytic therapy
Results from the SAMPA randomized trial
Figure 1. (A) Temporal trends in first medical contact to fibrinolytic therapy. (B) Temporal trends in first medical contact to PCI. IQR, interquartile range; MP, metropolitan; NM, nonmetropolitan; PCI, percutaneous coronary intervention.
Method (1)
Registry e-MUST, *For the e-MUST investigators*
www.cardio-arsif.org

– Data from an ongoing prospective registry that includes all STEMI managed by MICUs in the Greater Paris Area.

– Prehospital System:
  • 8 SAMU, 40 SMUR, Dispatching Center « 15 »
– STEMI < 12h
– 2008 -2012
– All patients: from scene to cath-lab hospital)
Results (2): «Real Life» vs ESC guidelines

STEMI <2h
(66% STEMI <12h)

City of Paris
Small ring only
Large ring only

STEMI 2-12h
(34% STEMI <12h)

Great Paris Area
2008-2012

Y. Lambert & e-MUST study group, unpublished data
Results (4): Hospital mortality

Without critical factor
87 (1.9%)

« early presenter »

STEMI <2h
54 (1.8%)

PI
4 (0.8%)
pPCI <60'
3 (2.1%)
pPCI 60-120'
34 (1.6%)
pPCI >120'
13 (4.0%)

P = 0.14
P = 0.005

STEMI 2-12h
33 (2.1%)

PI
1 (1.1%)
pPCI <90'
12 (1.7%)
pPCI 90-120'
11 (2.0%)
pPCI >120'
9 (4.2%)

P = 0.575
P = 0.029

Y. Lambert & e-MUST study group, unpublished data
Fibrinolysis or Primary PCI in ST-Segment Elevation Myocardial Infarction

Paul W. Armstrong, M.D., Anthony H. Gershlick, M.D., Patrick Goldstein, M.D., Robert Wilcox, M.D., Thierry Danays, M.D., Yves Lambert, M.D., Vitaly Sulimov, M.D., Ph.D., Fernando Rosell Ortiz, M.D., Ph.D., Miodrag Ostojic, M.D., Ph.D., Robert C. Welsh, M.D., Antonio C. Carvalho, M.D., Ph.D., John Nanas, M.D., Ph.D., Hans-Richard Arntz, M.D., Ph.D., Sigrun Halvorsen, M.D., Ph.D., Kurt Huber, M.D., Stefan Grajek, M.D., Ph.D., Claudio Fresco, M.D., Erich Bluhmki, M.D., Ph.D., Anne Regelin, Ph.D., Kathleen Vandenberghhe, Ph.D., Kris Bogaerts, Ph.D., and Frans Van de Werf, M.D., Ph.D., for the STREAM Investigative Team*
All-cause mortality before & after amendment

Patients randomized before Am. (n=382)  Patients randomized after Am. (n=1,510)

Cumulative incidence (%)

<table>
<thead>
<tr>
<th>Months since randomization</th>
<th>TNK 9.9%</th>
<th>PPCI 4.3%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
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<tr>
<td>4</td>
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<td>5</td>
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<td>6</td>
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<td>10</td>
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<tr>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Log-Rank Test p=0.032

RR = 2.32
(95% CI 1.01-8.31)
p=0.048

RR = 0.93
(95% CI 0.60-1.43)
p=0.731

Number at risk:
- TNK
  - before Am.: 193
  - after Am.: 751
- Primary PCI
  - before Am.: 169
  - after Am.: 739

Number at risk:
- TNK
  - before Am.: 175
  - after Am.: 719
- Primary PCI
  - before Am.: 179
  - after Am.: 718

TNK 5.9%
PPCI 6.3%
STREAM  Group A Aborted MI

<table>
<thead>
<tr>
<th>Baseline ECG</th>
<th>Randomization</th>
<th>TNK</th>
<th>90min post T ECG</th>
</tr>
</thead>
<tbody>
<tr>
<td>- 18</td>
<td>- 7</td>
<td>0</td>
<td>91</td>
</tr>
<tr>
<td>12:22</td>
<td>12:33</td>
<td>12:40</td>
<td>14:11</td>
</tr>
</tbody>
</table>

11 July 2009
AbMI Clinical Outcomes by Rx Group

<table>
<thead>
<tr>
<th>AbMI (N=158)</th>
<th>Non AbMI (N=1596)</th>
<th>Relative Risk (95%CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of events/total no. of patients (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Composite of death/shock/CHF/reMI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Group A</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5/99(5.1)</td>
<td>95/790(12.0)</td>
<td>Unadjusted</td>
<td>0.42(0.18-1.01)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adjusted*</td>
<td>0.43(0.16-1.15)</td>
</tr>
<tr>
<td><strong>Group B</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6/59(10.2)</td>
<td>103/799(12.9)</td>
<td>Unadjusted</td>
<td>0.79(0.36-1.72)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adjusted*</td>
<td>0.76(0.36-1.61)</td>
</tr>
</tbody>
</table>

Maleki et al  Heart 2014
Impact on Cardiogenic Shock of Fibrinolysis before PCI

Figure 1: Incidence of cardiogenic shock in fibrinolysis pre-PCI vs. primary PCI.

<table>
<thead>
<tr>
<th>Study</th>
<th>Fibrinolysis pre-PCI (n)</th>
<th>Primary PCI (n)</th>
<th>Relative Risk (95% CI)</th>
<th>Fibrinolysis pre-PCI better</th>
<th>Fibrinolysis pre-PCI worse</th>
</tr>
</thead>
<tbody>
<tr>
<td>STREAM</td>
<td>41/939</td>
<td>56/944</td>
<td>0.74 (0.50-1.09)</td>
<td>p=0.12</td>
<td></td>
</tr>
<tr>
<td>FINESSE</td>
<td>44/828</td>
<td>55/806</td>
<td>0.78 (0.53-1.14)</td>
<td>p=0.20</td>
<td></td>
</tr>
<tr>
<td>WEST</td>
<td>4/104</td>
<td>7/100</td>
<td>0.55 (0.17-1.82)</td>
<td>p=0.32</td>
<td></td>
</tr>
<tr>
<td>CAPTIM</td>
<td>10/419</td>
<td>20/421</td>
<td>0.50 (0.24-1.06)</td>
<td>p=0.06</td>
<td></td>
</tr>
<tr>
<td>ASSENT-4 PCI</td>
<td>51/807</td>
<td>39/817</td>
<td>1.32 (0.88-1.99)</td>
<td>p=0.17</td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>150/3097</td>
<td>177/3088</td>
<td>0.84 (0.68-1.04)</td>
<td>p=0.12</td>
<td></td>
</tr>
<tr>
<td>Patients &lt;3h</td>
<td>69/1678</td>
<td>106/1624</td>
<td>0.63 (0.47-0.84)</td>
<td>p=0.002</td>
<td></td>
</tr>
</tbody>
</table>
Other lessons learned from the French surveys
Role of PCI after PHT
FAST-MI: 30-day mortality according to early PCI after pre-hospital lysis

87% of the patients with PCI during hospital stay

- Clinically driven PCI
  - PCI <= 3h: 3.1%
  - PCI 3-24 hrs: 4.0%
  - Late PCI: 0%

- Routine PCI
  - 56% mortality
  - 55% mortality
  - 59% mortality

FAST-MI 2007
Meeting the requirements of the guidelines influences survival

<table>
<thead>
<tr>
<th>% in-hospital death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,1</td>
</tr>
<tr>
<td>3,5</td>
</tr>
</tbody>
</table>

Adjusted OR: 2.92 (1.17-7.30)
P = 0.02

Median time from ECG to PCI: 110 min [78; 185]
Only 55% met the recommended timelines
NON STEMI...................really serious
Baseline ECG & MACE at 30 days

% Event rate (Death / AMI / refractory angina) at 30 days (95% CI)

- ST-depression: 21% (12-30%)
- Non-evaluable ECG: 12% (4-20%)
- Inverted T-waves: 10% (6-14%)
- All patients: 10% (6-14%)
- Normal ECG: 8% (4-12%)
- ST-elevation: 7% (2-12%)

Holmvang et al. TRIM study Am Heart J 1999;137:24-33
Magnitude of ST-segment depression & Prognosis

Event rate at 30 days (95% CI) (%)

ST-depression magnitude (summed)

- Minor 2 – 3 mm: (1-19%) (4-26%)
- Intermediate 3.5 – 5 mm: (-3-29%) (0-38%)
- Major > 5 mm: (7-51%) (12-58%)

Distribution of magnitude of ST-segment depression in relation to cardiac events at 30 days

Holmvang et al. TRIM study

Am Heart J 1999;137:24-33
Thrombolysis in Myocardial Ischemia (TIMI) trial
Patients presenting without ST-segment elevation on the electrocardiogram
To reduce diagnostic time...
Pretreatment with Prasugrel in Non-ST-Segment Elevation Acute Coronary Syndromes

Gilles Montalescot, M.D., Ph.D., Leonardo Bolognese, M.D., Dariusz Dudek, M.D., Ph.D., Patrick Goldstein, M.D., Christian Harmm, M.D., Jean-Francois Tanguay, M.D., Jurrien M. ten Berg, M.D., Ph.D., Debra L. Miller, R.N., Timothy M. Costigan, Ph.D., Jochen Goedicke, M.D., Johanne Silvain, M.D., Ph.D., Paolo Angioli, M.D., Jacek Legutko, M.D., Ph.D., Margit Niethammer, M.D., Zuzana Motovska, M.D., Ph.D., Joseph A. Jakubowski, Ph.D., Guillaume Cayla, M.D., Ph.D., Luigi Oltrona Visconti, M.D., Eric Vicaud, M.D., Ph.D., and Petr Widimsky, M.D., D.Sc., for the ACCOAST Investigators*

ABSTRACT

From Institut de Cardiologie, Centre Hospitalier Universitaire Pitié-Salpêtrière (ACTION group, Assistance Publique–Hôpitaux de Paris [AP-HP], Université Paris 6) (G.M., J.S.) and Methodology and Statistical Unit, Centre Hospitalier Universitaire Lariboisière (ACTION group, AP-HP, Université Paris 7) (E.V.), Paris, and Ser-
No. at Risk, Primary Efficacy End Point:
No pre-treatment
Pre-treatment

Efficacy End Point @ 7 + 30 days (All Patients)

CV Death, MI, Stroke, UR, GPIIb/IIIa Bailout

Pre-treatment
No Pre-treatment

Hazard Ratio, 1.02
(95% 0.84, 1.25)
P=0.81

Hazard Ratio, 0.997
(95% 0.83, 1.20)
P=0.98
All TIMI (CABG or non-CABG) Major Bleeding
(All Treated patients)

No. at Risk, All TIMI Major Bleeding:
No pre-treatment 1996
Pre-treatment 2037

Endpoints (%):
Pre-treatment 2.6
No Pre-treatment 1.4
Pre-treatment 2.9
No Pre-treatment 1.5

Hazard Ratio, 1.90
(95% CI 1.19, 3.02)
P = 0.006

Hazard Ratio, 1.97
(95% CI 1.26, 3.08)
P = 0.002

Days From First Dose
0 5 10 15 20 25 30
At this moment

Only one antiplatelet agent in the emergency area
- for STEMI?
- for high-risk NSTEMI?
- for all NSTEMI?????
And for inter-hospital transfer?
<table>
<thead>
<tr>
<th>Recommendations for platelet inhibition in NSTE-ACS</th>
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<tbody>
<tr>
<td><strong>Oral antiplatelet therapy</strong></td>
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<tr>
<td>Aspirin is recommended for all patients without contraindications at an initial oral loading dose(^c) of 150–300 mg (in aspirin-naive patients) and a maintenance dose of 75–100 mg/day long-term regardless of treatment strategy.</td>
</tr>
<tr>
<td>A P2Y(_{12}) inhibitor is recommended, in addition to aspirin, for 12 months unless there are contraindications such as excessive risk of bleeds.</td>
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<tr>
<td>- Ticagrelor (180 mg loading dose, 90 mg twice daily) is recommended, in the absence of contraindications(^d), for all patients at moderate-to high-risk of ischaemic events (e.g., elevated cardiac troponins), regardless of initial treatment strategy and including those pretreated with clopidogrel (which should be discontinued when ticagrelor is started).</td>
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<tr>
<td>- Prasugrel (60 mg loading dose, 10 mg daily dose) is recommended in patients who are proceeding to PCI if no contraindication.(^d)</td>
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<td>- Clopidogrel (300–600 mg loading dose, 75 mg daily dose) is recommended for patients who cannot receive ticagrelor or prasugrel or who require oral anticoagulation.</td>
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<td>P2Y(_{12}) inhibitor administration for a shorter duration of 3–6 months after DES implantation may be considered in patients deemed at high bleeding risk.</td>
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<td>It is not recommended to administer prasugrel in patients in whom coronary anatomy is not known.</td>
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<td><strong>Intravenous antiplatelet therapy</strong></td>
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<td>GPIIb/IIIa inhibitors during PCI should be considered for bailout situations or thrombotic complications.</td>
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<td>Cangrelor may be considered in P2Y(_{12}) inhibitor-naive patients undergoing PCI.</td>
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<tr>
<td>It is not recommended to administer GPIIb/IIIa inhibitors in patients in whom coronary anatomy is not known.</td>
</tr>
<tr>
<td>Recommendations</td>
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<td>---------------------------------------------------------------------------------</td>
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</tbody>
</table>
| An **immediate invasive strategy (<2h)** is recommended in patients with at least one of the following very-high-risk criteria:  
  - haemodynamic instability or cardiogenic shock  
  - recurrent or ongoing chest pain refractory to medical treatment  
  - life-threatening arrhythmias or cardiac arrest  
  - mechanical complications of MI  
  - acute heart failure with refractory angina or ST deviation  
  - recurrent dynamic ST- or T-wave changes, particularly with intermittent ST-elevation. | I     | C     |
| An **early invasive strategy (<24h)** is recommended in patients with at least one of the following high-risk criteria:  
  - rise or fall in cardiac troponin compatible with MI  
  - dynamic ST- or T-wave changes (symptomatic or silent)  
  - GRACE score >140. | I     | A     |
| An **invasive strategy (<72h)** is recommended in patients with:  
  - at least one of the following intermediate-risk criteria:  
    - diabetes mellitus  
    - renal insufficiency (eGFR <60 mL/min/1.73 m²)  
    - LVEF <40% or congestive heart failure  
    - early post-infarction angina  
    - recent PCI  
    - prior CABG  
    - GRACE risk score >109 and <140  
  or  
  - recurrent symptoms or ischaemia on non-invasive testing. | I     | A     |
| In patients with none of the mentioned risk criteria and no recurrent symptoms, non-invasive testing for ischaemia (preferably with imaging) is recommended before deciding on invasive evaluation. | I     | A     |
| In centres experienced with radial access, a radial approach is recommended for coronary angiography and PCI. | I     | A     |
| In patients undergoing PCI, new-generation DESs are recommended. | I     | A     |
Non STEMI guidelines ESC 2015