Αντιπαράθεση
Σταθερή στηθάγχη: φάρμακα ή ΕΠΑΝΑΓΓΕΙΩΣΗ

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Disclosures

• Speaker fees: Boehringer Ingelheim, Galenica, Bayer, Elpen, Minerva, Lilly
Angina is the most obvious clinical manifestation of myocardial ischaemia.

PCI is a method to decrease angina episodes, but doing so, however, does not always relieve ischaemia.
The optimal treatment strategy, percutaneous coronary intervention (PCI) or medical therapy alone for patients with stable coronary disease remains controversial.
nonfatal myocardial infarction survival

PubMed from 1970 to October 2017

J Am Heart Assoc. 2017;6:e007006
Mitchell J. et al.
Post-trial survival information was available for 1211 patients, or 53% of the original study population, for a median follow-up of 11.9 years. → no late benefit in survival
Visual angiographic assessment vs FFR in the FAME trial

Tonino et al, J Am Coll Cardiol 2010;55:2816-21
Stable CAD patients scheduled for 1, 2 or 3 vessel DES-PCI  
N = 1220

Randomized Trial  
At least 1 stenosis with FFR ≤ 0.80 (n=888)  
Randomization 1:1  
PCI + MT  
MT  

73%  

Registry  
When all FFR > 0.80 (n=332)  
MT  

27%  

50% randomly assigned to FU  

Follow-up after 1, 6 months, 1, 2, 3 and 5 years
FAME 2: Initial Results

Primary Endpoint: Composite of Death, MI, or Urgent Revascularization

- PCI+MT vs. MT: HR 0.32 (0.19-0.53); p<0.001
- PCI+MT vs. Registry: HR 1.29 (0.49-3.39); p=0.61
- MT vs. Registry: HR 4.32 (1.75-10.7); p<0.001

FAME 2: Two Year Results

Primary Endpoint: Composite of Death, MI, or Urgent Revascularization

Objective

- Evaluate the long-term clinical outcomes, effects on quality of life, and cost-effectiveness of FFR-guided PCI versus medical therapy alone in patients with stable coronary artery disease enrolled in the FAME 2 trial.
Three Year Rate of Death, MI, or Urgent Revascularization

MT alone vs. PCI+MT:
Hazard ratio, 2.36 (95% CI, 1.66–3.36); P<0.001 by log-rank test

MT alone vs. Registry:
Hazard ratio, 1.89 (95% CI, 1.18–3.03); P=0.007 by log-rank test

PCI+MT vs. Registry:
Hazard ratio, 0.79 (95% CI, 0.47–1.33); P=0.38 by log-rank test

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>MT alone</td>
<td>0</td>
</tr>
<tr>
<td>PCI+MT</td>
<td>0</td>
</tr>
<tr>
<td>Registry</td>
<td>0</td>
</tr>
</tbody>
</table>
# Results: Clinical Outcome

## Three Year Rate of Death, MI, or Urgent Revascularization

<table>
<thead>
<tr>
<th>Event</th>
<th>Randomized trial N=888</th>
<th>P value</th>
<th>Registry N=322</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCI+MT=447</td>
<td>MT=441</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MACE</strong></td>
<td>10.1%</td>
<td>22%</td>
<td>12.7%</td>
</tr>
<tr>
<td><strong>Death</strong></td>
<td>2.7%</td>
<td>3.6%</td>
<td>3.0%</td>
</tr>
<tr>
<td><strong>Myocardial Infarction (MI)</strong></td>
<td>6.3%</td>
<td>7.7%</td>
<td>6.6%</td>
</tr>
<tr>
<td><strong>Death or MI</strong></td>
<td>8.3%</td>
<td>10.4%</td>
<td>9.0%</td>
</tr>
<tr>
<td><strong>Urgent Revascularization</strong></td>
<td>4.3%</td>
<td>17.2%</td>
<td>6.6%</td>
</tr>
</tbody>
</table>
Results: Quality of Life

% of Patients with Class II-IV Angina at each Time Point

<table>
<thead>
<tr>
<th>Time Point</th>
<th>PCI+MT</th>
<th>MT alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>70.2%</td>
<td>67.7%</td>
</tr>
<tr>
<td>1 Month</td>
<td>10.2%</td>
<td>28.5%</td>
</tr>
<tr>
<td>6 Months</td>
<td>7.5%</td>
<td>18.4%</td>
</tr>
<tr>
<td>1 Year</td>
<td>5.9%</td>
<td>15.2%</td>
</tr>
<tr>
<td>2 Years</td>
<td>5.9%</td>
<td>12%</td>
</tr>
<tr>
<td>3 Years</td>
<td>5.2%</td>
<td>9.7%</td>
</tr>
</tbody>
</table>

P-values:
- Baseline: P=0.42
- 1 Month: P<0.001
- 6 Months: P<0.001
- 1 Year: P<0.001
- 2 Years: P=0.002
- 3 Years: P=0.015
Results: Quality of Life

Mean Number of Antianginal Medications/Patient at each Time Point

<table>
<thead>
<tr>
<th>Time Point</th>
<th>PCI+MT</th>
<th>MT alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>1.33</td>
<td>1.35</td>
</tr>
<tr>
<td>1 Month</td>
<td>1.36</td>
<td>1.79</td>
</tr>
<tr>
<td>6 Months</td>
<td>1.32</td>
<td>1.68</td>
</tr>
<tr>
<td>1 Year</td>
<td>1.35</td>
<td>1.62</td>
</tr>
<tr>
<td>2 Years</td>
<td>1.36</td>
<td>1.53</td>
</tr>
<tr>
<td>3 Years</td>
<td>1.29</td>
<td>1.52</td>
</tr>
</tbody>
</table>
Results: Quality of Life

EQ-5D Results at each Time Point

*P<0.05 compared with baseline.
Conclusion

- Compared with best medical therapy alone, performing PCI in patients with stable CAD and at least one coronary lesion with an abnormal FFR leads to improved clinical outcome, less angina, and improved quality of life at similar cost over three years of follow-up.
Objective Randomised Blinded Investigation with optimal medical Therapy of Angioplasty in stable angina (ORBITA)

- **Enrolment assessment**
  - Demographics
  - CCS Questionnaires
  - Blood pressure, heart rate

- **Medical optimisation phase**
  - 6 weeks

- **Pre-randomisation assessment**
  - CCS Questionnaires
  - CPET
  - DSE
  - Blood pressure, heart rate

- **Blinded procedure**
  - Research angiogram
  - iFR, FFR
  - Sedation
  - PCI

- **Randomisation**
  - Placebo

- **Blinded follow-up phase**
  - 6 weeks

- **Follow-up assessment**
  - CCS Questionnaires
  - CPET
  - DSE
  - Blood pressure, heart rate
Primary endpoint result

Change in total exercise time

PCI

+16.6 sec
(-8.9 to 42.0)
p=0.200

Placebo

28.4
(SD 86.3)
p=0.001

11.8
(SD 93.3)
p=0.235
**Secondary endpoint results**

**Blinded evaluation of ischaemia reduction**

<table>
<thead>
<tr>
<th>Peak stress wall motion index score</th>
<th>PCI</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-randomization</td>
<td>1.11 (0.18)</td>
<td>1.11 (0.18)</td>
</tr>
<tr>
<td>Follow-up</td>
<td>1.03 (0.06)</td>
<td>1.13 (0.19)</td>
</tr>
<tr>
<td>Δ (Pre-randomization to follow-up)</td>
<td>-0.08 (0.17)</td>
<td>0.02 (0.16)</td>
</tr>
<tr>
<td><em>p</em></td>
<td>*&lt;*0.0001</td>
<td>0.433</td>
</tr>
</tbody>
</table>

**Difference in Δ between arms**

-0.09 (-0.15 to -0.04)

*p*=0.0011

PCI did significantly improve the dobutamine stress echo wall-motion index, indicating that stenting reduced ischemic burden.
The 2 gladiators..

**ORBITA**
- 200 pts
- Mostly Single vessel
- FU 6 weeks
- Sham operation
- 28%-32% of randomized subjects had either normal FFR or IFR
- End points→ symptomatic and exercise test improvements

**FAME 2**
- 1220 (889) pts
- Multivessel disease
- FU 3 years
- Cath and FFR to all of the pts
- End points: interim data → substantially fewer events related to the primary composite endpoint of all-cause death, MI, or urgent revascularization in the FFR-guided group.
COURAGE + FAME = FAME 2

- ORBITA + FAME 2
  1. 1\textsuperscript{st} line OMT
  2. 2\textsuperscript{nd} line OMT
  3. Refractory angina, multivessel disease—PCI
  4. SHAM operation and blinded trials are really necessary in the current era
The purpose of the ISCHEMIA trial is to determine the best management strategy for higher-risk patients with stable ischemic heart disease.

This is a multicenter randomized controlled trial with a target enrollment of ~5000 patients with at least moderate ischemia on stress testing.

Patients are assigned at random to a routine invasive strategy (INV) with cardiac catheterization followed by revascularization plus optimal medical therapy (OMT) or to a conservative strategy (CON) of OMT, with cardiac catheterization and revascularization reserved for those who fail OMT.

### Study Design

- **Study Type**: Interventional (Clinical Trial)
- **Estimated Enrollment**: 5000 participants
- **Allocation**: Randomized
- **Intervention Model**: Parallel Assignment
- **Masking**: None (Open Label)
- **Primary Purpose**: Treatment
- **Official Title**: International Study of Comparative Health Effectiveness With Medical and Invasive Approaches (ISCHEMIA)
- **Study Start Date**: July 2012
- **Estimated Primary Completion Date**: December 2018
- **Estimated Study Completion Date**: December 2018
CA does not always speak the truth
before PCI think twice
# Revascularization of SCAD patients on OMT

(Adapted from the ESC/EACTS 2010 Guidelines)

<table>
<thead>
<tr>
<th>Indication</th>
<th>To improve prognosis</th>
<th>To improve symptoms persistent on OMT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Class</td>
<td>Level</td>
</tr>
<tr>
<td>A Heart Team approach to revascularization is recommended in patients with unprotected left main, 2–3 vessel disease, diabetes or comorbidities.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Left main &gt;50% diameter stenosis.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Any proximal LAD &gt;50% diameter stenosis.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>2–3 vessel disease with impaired LV function/CHF.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Single remaining vessel (&gt;50% diameter stenosis*).</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Proven large area of ischaemia (&gt;10% LV6)</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Any significant stenosis with limiting symptoms or symptoms non responsive/intolerant to OMT.</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Dyspnoea/cardiac heart failure with &gt;10% ischaemia/viability supplied by stenosis &gt;50%</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>No limiting symptoms with OMT in vessel other than left main or proximal LAD or single remaining vessel or vessel subtending area of ischaemia &lt;10% of myocardium or with FFR ≥0.80.</td>
<td>III</td>
<td>A</td>
</tr>
</tbody>
</table>

CHF = congestive heart failure; FFR = fractional flow reserve; LAD = left anterior descending; LV = left ventricular; OMT = optimal medical therapy; SCAD = stable coronary artery disease. *In asymptomatic patients, the decision will be guided by the extent of ischaemia on stress testing. With documented ischaemia or FFR <0.80 for angiographic diameter stenoses 50–90%. †As assessed by non-invasive test (SPECT, MRI, stress echocardiography).

This slide corresponds to Table 32 in the full text.
Conclusions

First line therapy for management of stable CAD includes lifestyle modification, dietary changes, exercise, smoking cessation, and aggressive medical therapy for control of lipids, hypertension, and diabetes.

Optimal medical therapy remains the cornerstone for treatment of patients with stable CAD.

PCI has an important role in treating patients with angina refractory to medical therapy.

The three year results of the FAME 2 study demonstrate that FFR-guided stenting significantly improves the quality of life of patients with stable coronary disease at no additional cost when compared with medical therapy alone.

Orbita demonstrated that a placebo/sham control for PCI therapy is possible.

FFR has become to coronary physiology what ejection fraction is to left ventricular function.

“Oculostenotic” reflex to an “ischemia-PCI” reflex.
I need MT but PCI following FFR is making the difference

Thank you!!