# AMERICA

**AMERICA investigators**

**www.action-coeur.org**

Aggressive detection and Management of the Extension of atherothrombosis in high Risk coronary patients In comparison with standard of Care for coronary Atherosclerosis
The AMERICA study

# Disclosures

- Research grants from Bristol-Myers Squibb, Sanofi-Aventis, Eli Lilly, Guerbet Medical, Medtronic, Boston Scientific, Cordis, Stago, Centocor, Fondation de France, INSERM, Federation Francaise de Cardiologie, and Société Française de Cardiologie;
- Consulting fees from Sanofi-Aventis, Eli Lilly, and Bristol-Myers Squibb; and lecture fees from Bristol-Myers Squibb, Sanofi-Aventis, and Eli Lilly.

# AMERICA: Study organization

**ACTION Study Group (www.action-coeur.org)**

- **Academic Coordinating Center**: Institute of Cardiology - Pitié-Salpêtrière, Paris
- **Academic Sponsor**: AP-HP, Paris
- **Academic Global Trial Operations**: URC - Lariboisière, Paris

- **Funding**: ACTION, Institut de l'Athérothrombose
- **Steering Committee**: G. Montalescot, JP Collet, G. Cayla, E. Vicaut,
- I**nvestigation sites** : 28 French Intervention Centers

# AMERICA Study: Rationale (1)

- **Coronary artery disease**→ the most frequent and severe location of atherosclerosis
- **Symptomatic multisite artery disease** (**MSAD**) → integrator of the global CV risk
- The prevalence and associated-risk of **asymptomatic MSAD** in high risk coronary patients are unknown.
- Whether **systematic identification of MSAD and treatment** when appropriate combined with an aggressive secondary prevention is relevant has not been evaluated.

# AMERICA Study: Rationale (2)

- To demonstrate the **superiority** of a **pro-active strategy** of detection and management of the extension of atherothrombosis to other territories than coronary combined with an aggressive pharmacological secondary prevention strategy in a population with very high risk features of coronary disease (**pro-active strategy**)
- As compared with a **conservative strategy** based on a clinically-guided identification of MSAD and standard pharmacological treatment (**conventional strategy**).

# Study Design

**Three vessels disease ≥18 years old (≤ 6 months)**
**and/or**
**Acute coronary syndrome ≥75 years old (<1month)**

## Pro-Active Strategy

- **Active detection/management of asymptomatic atherothrombosis**
  - **Total body vascular doppler ultrasound investigatioincombined with CTA or MRI if needed**
  - **Anckle brachial index measure**
  - **Creatinine clearance, fasting glycemia, LDL-cholesterol every 6 months**
- **Intensive medical therapy**
  - **Dual antiplatelet therapy during whole follow-up**
  - **High dose statin**
  - **Systematic beta-blockade and ACE inhibition irrespective of LEVF**
  - **Anti-aldosterone blockade after MI if LEVF≤40%**
  - **Smoking cessation and rehabilitation programs**

## Conventional Strategy

- **No detection of asymptomatic atherothrombosis**
- **Standard medical therapy**

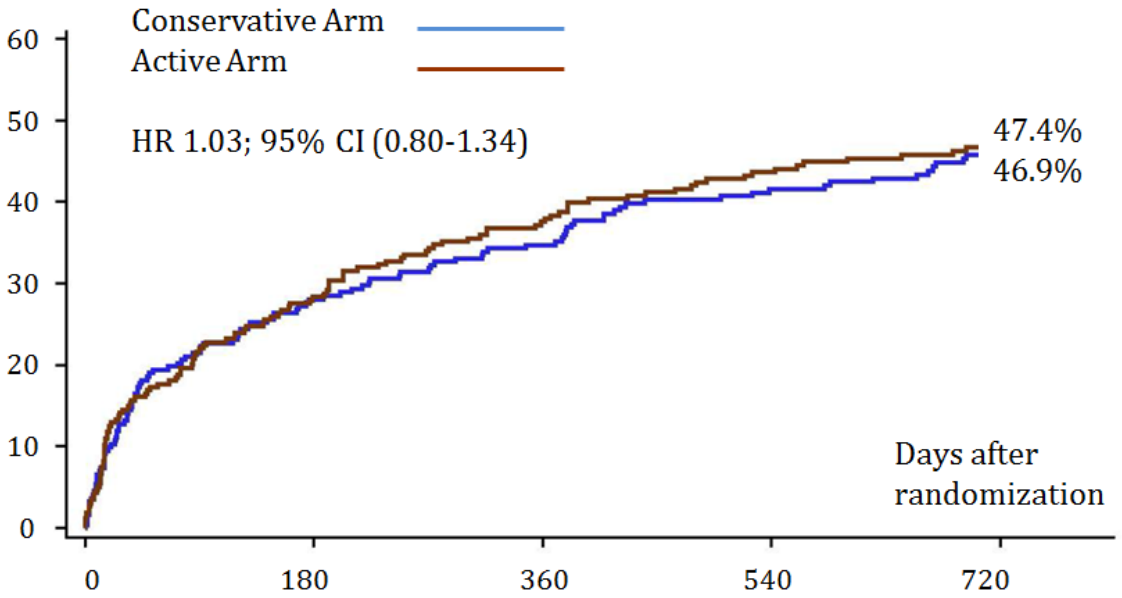
**Occurrence of Primary endpoint during the two year follow up**

- Death (any cause)
- Any ischemic event leading to hospitalization
- Evidence of organ failure

| Baseline Characteristics | Pro-active group (n=263) | Conventional group (n=258) |
|---|---|---|
| ACS in elderly (%) | 43% | 40% |
| Age: mean (→ %>75) | 77.7 (60%) | 76.0 (58%) |
| Women | 76 (28.9%) | 67 (26.0%) |
| Current smoker | 38 (14.4%) | 35 (13.6%) |
| Hypertension | 170 (64.6%) | 180 (69.8%) |
| Diabetes | 71 (27.0%) | 63 (24.4%) |
| Dyslipidemia | 147 (55.9%) | 150 (58.1%) |
| Severe renal failure | 9 (3.4%) | 11 (4.3%) |
| Prior myocardial infarction | 52 (19.8%) | 62 (24.0%) |
| Prior PCI | 54 (20.5%) | 61 (23.6%) |
| Peripheral artery disease | 22 (8.4%) | 28 (10.9%) |
| Prior Stroke | 20 (7.6%) | 13 (5.0%) |

# Primary Endpoint at 2 years-FU*

* death, any ischemic event leading to rehospitalization or any evidence of organ failure




| Subjects at risk | | | | | |
|---|---|---|---|---|---|
| Active arm | 263 | 181 | 156 | 135 | 97 |
| Conservative arm | 258 | 174 | 155 | 133 | 97 |

| Key secondary outcomes | Pro-active Arm (n=263) | Conventional Arm (n=258) | Hazard Ratio (95% CI) | p-value |
|---|---|---|---|---|
| **All-cause mortality** | **23 (8.7%)** | **28 (10.9%)** | **0.78 (0.45-1.35)** | **0.37** |
| Myocardial infarction | 36 (13.7%) | 25 (9.7%) | 1.39 (0.83-2.31) | 0.21 |
| Stroke | 6 (2.3%) | 5 (1.9%) | 1.13 (0.35-3.72) | 0.83 |
| Critical Limb ischemia | 6 (2.3%) | 1 (0.4%) | 5.73 (0.69-47.60) | 0.11 |
| AAA fissuration | 1 (0.4%) | 0 (0.0%) | | |
| Revascularization | 77 (29.3%) | 56 (21.7%) | 1.36 (0.96-1.91) | 0.083 |
| **PCI** | **63 (24.0%)** | **50 (19.4%)** | **1.21 (0.84-1.76)** | **0.31** |
| Coronary artery bypass graft | 17 (6.5%) | 8 (3.1%) | 2.04 (0.88-4.73) | 0.09 |
| **Organ failure** | **38 (14.4%)** | **37 (14.3%)** | **0.97 (0.62-1.53)** | **0.91** |

# Conclusions

- Asymptomatic MSAD is identified in one out of five high risk CAD patients

- AMERICA does not support the routine detection of asymptomatic MSAD even in high coronary risk patients as those recruited in the trial while aggressive secondary prevention strategy appears to be the standard of care already.