

Imaging & Physiology Summit: Outcome Data

FAME-2 Study: 2-year Results of FFR-guided PCI vs Medical Therapy

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FAME 2 Background

- In patients with stable coronary artery disease (CAD), PCI has not been shown to improve ‘hard endpoints’.
- In previous trials comparing PCI and Medical Therapy (MT), neither FFR-guidance nor DES were used. (‘contemporary PCI’).
- FFR guided PCI leads to 25-30% lower event rate than standard angiography guided PCI (*FAME study*)

—————→ FAME 2 Objective

To compare the rate of death, myocardial infarction, or urgent revascularization 2 years after contemporary PCI+MT to MT alone in stable CAD

FAME 2 Inclusion Criteria

**Angiographically defined 1, 2, or 3 VD
and**

Clinically stable CAD:

- Stable angina pectoris (CCS 1, 2, 3)
- Stabilized angina pectoris CCS class 4
- Silent ischemia

FAME 2 Exclusion Criteria

1. Prior CABG

2. LVEF < 30%

3. LM disease

FAME 2 Primary End Point

Two-year composite of:

- all cause death
- myocardial infarction
- urgent revascularization

FAME 2 Flow Chart

Stable CAD patients scheduled for 1, 2 or 3 vessel DES-PCI
N = 1220

FFR in all target lesions

Randomized Trial

Registry

At least 1 stenosis
with FFR ≤ 0.80 (n=888)

When all FFR > 0.80
(n=332)

Randomization 1:1

PCI + MT

MT

MT

73%

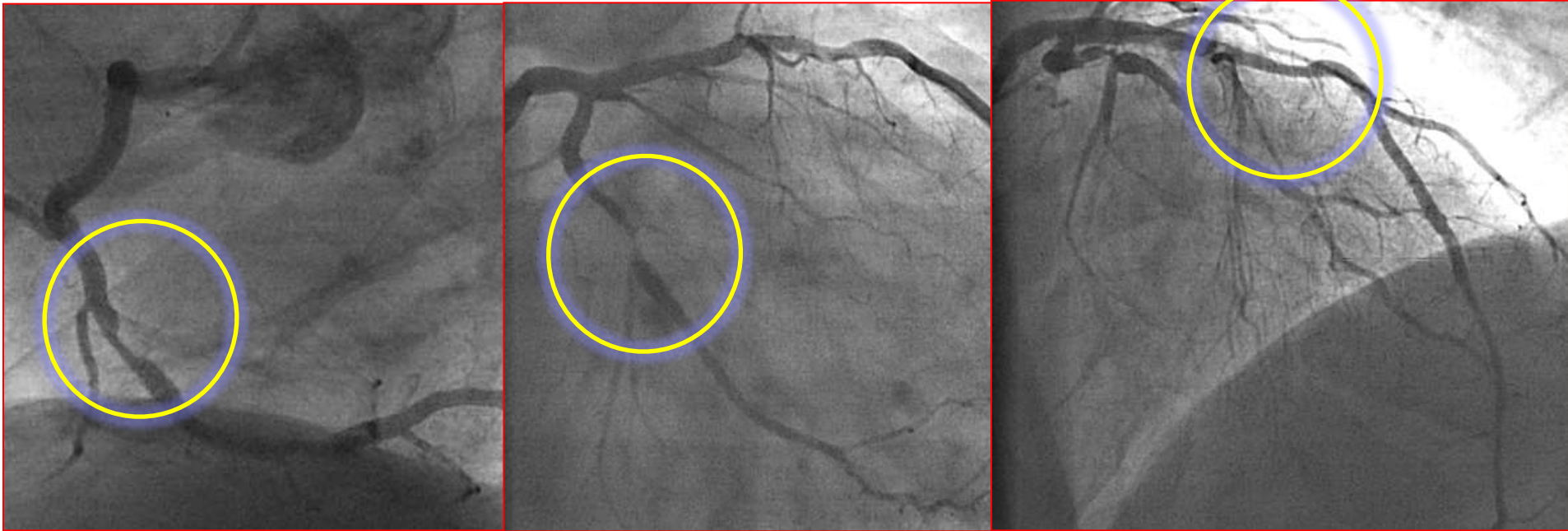
27%

50% randomly
assigned to FU

Follow-up after 1, 6 months, 1, 2, 3, 4, and 5 years

FAME 2 Illustrative Cases

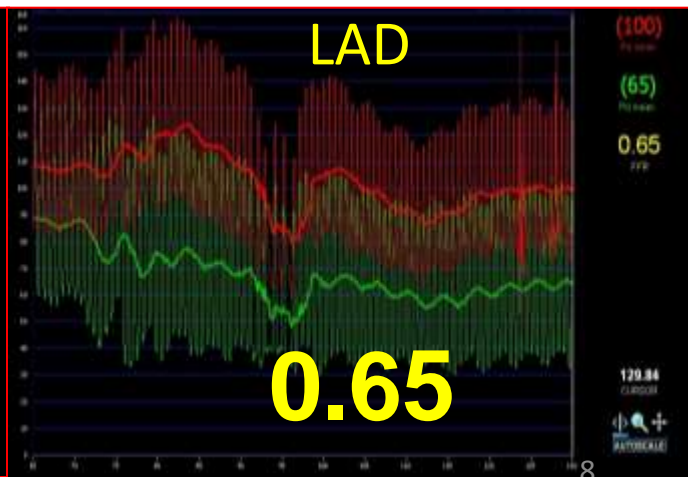
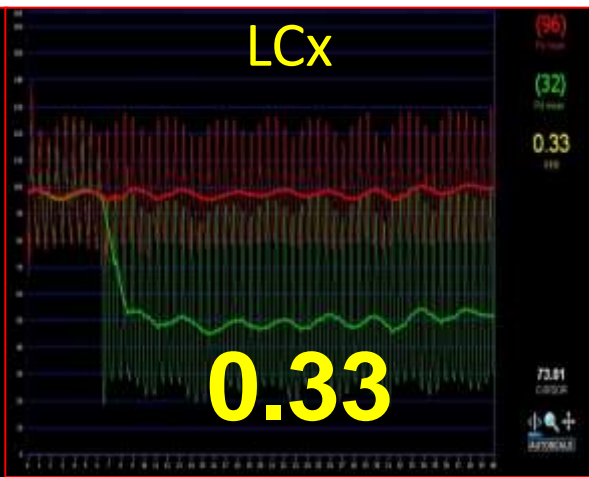
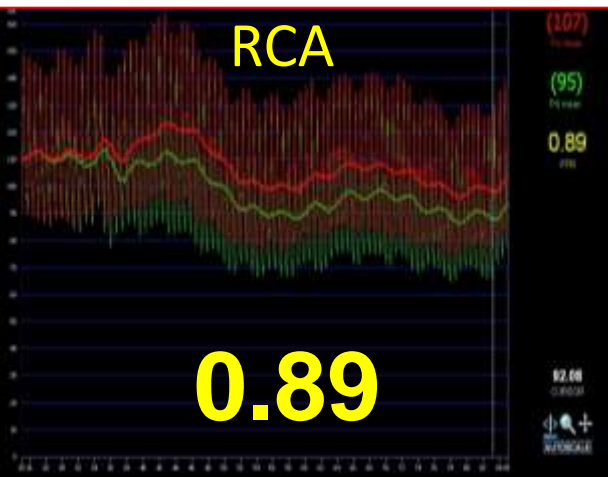
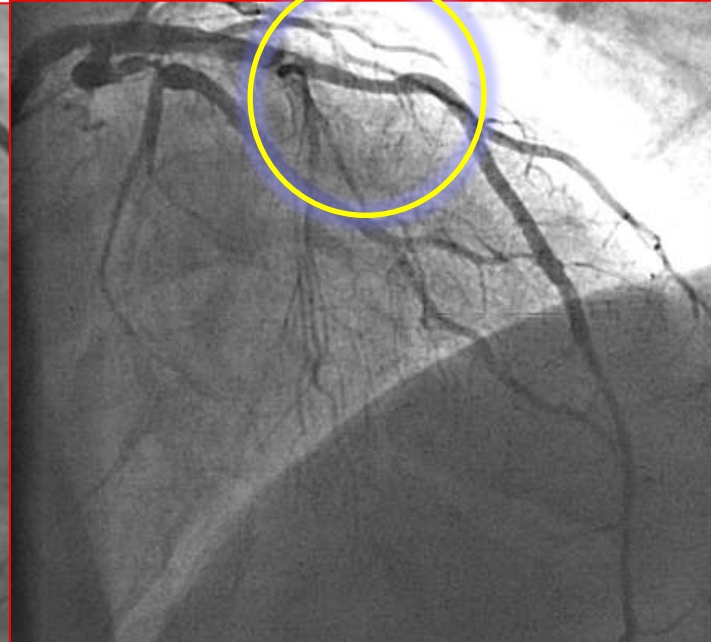
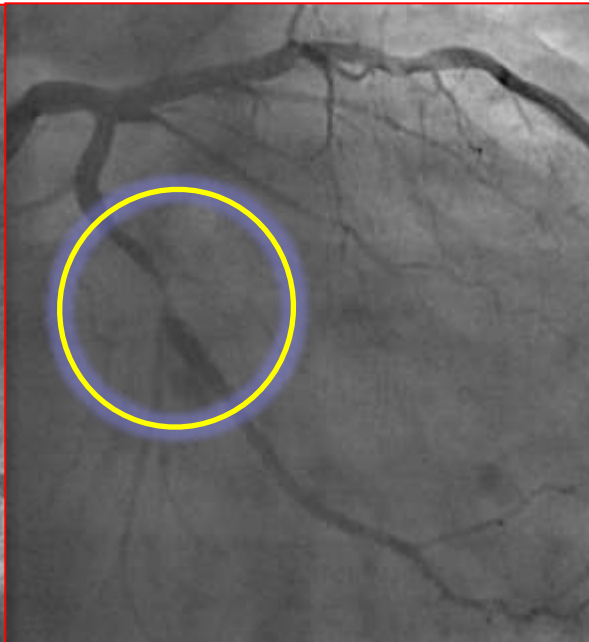
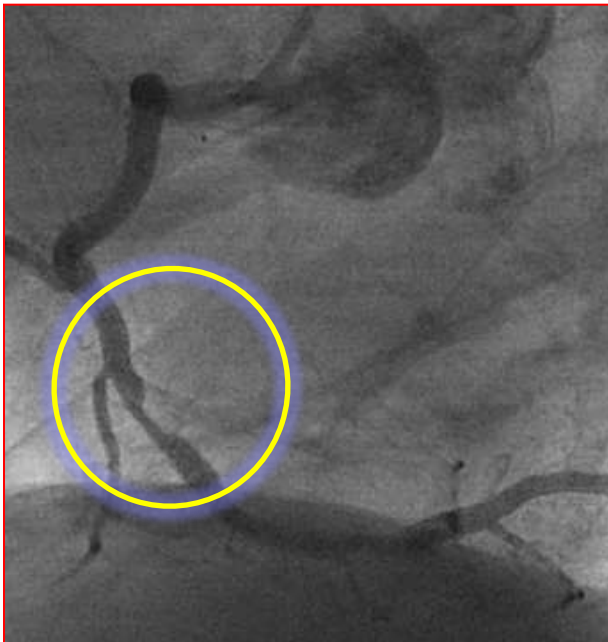
Case 1



- **58-year-old man with CCS 3**
- **Risk Factors**
 - Hyperlipidemia
 - Familial History
 - Arterial hypertension

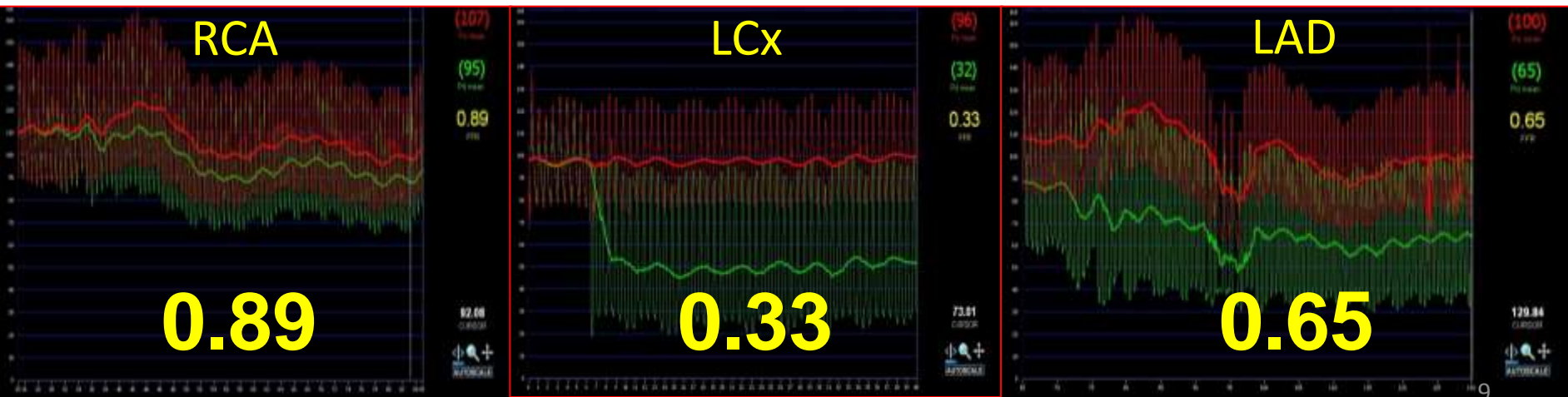
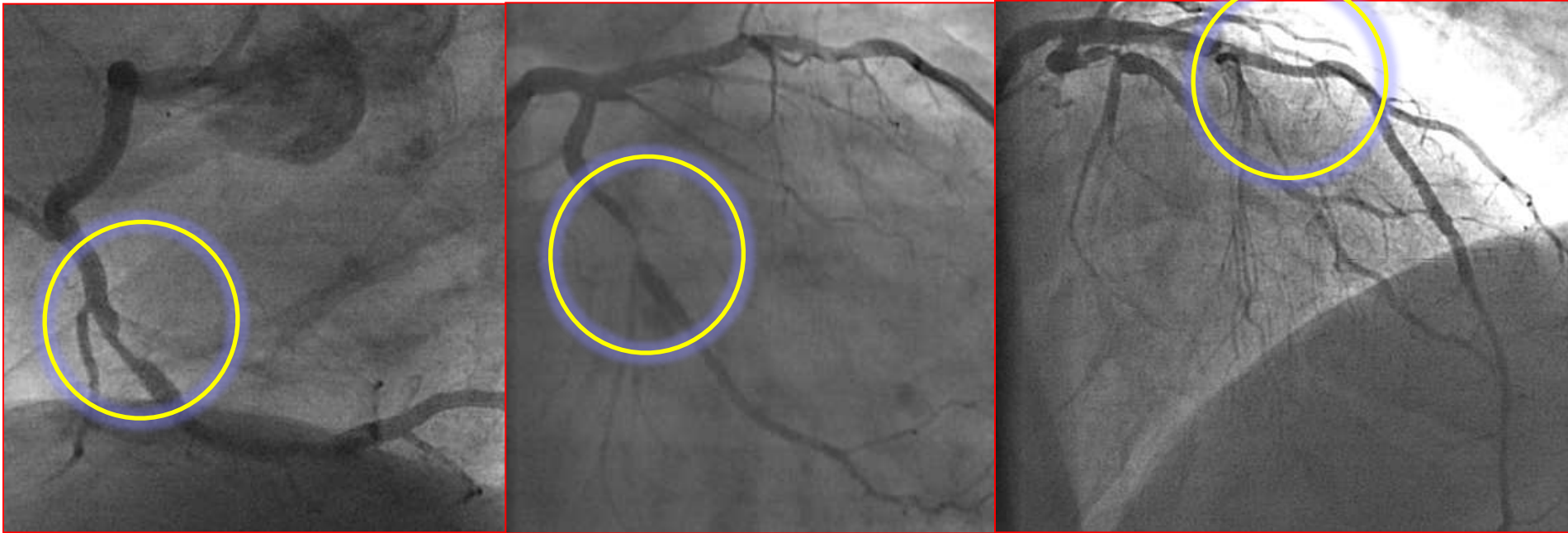
FAME 2 Illustrative Cases

Case 1



FAME 2 Illustrative Cases

Case 1 → randomized trial



DSMB Recommendation

On recommendation of the independent Data and Safety Monitoring Board*, recruitment was halted on January 15th, 2012 after inclusion of 1220 patients (\pm 54% of the initially planned number of randomized patients)

****DSMB: Stephan Windecker, Chairman, Stuart Pocock, Bernard Gersh***

FAME 2 Baseline Clinical Characteristics (1&2)

There were no differences between the groups (PCI vs OMT vs Registry) with respect to clinical & baseline characteristics, age, angina class, risk factors, neither any angiographic differences.

FAME 2 FFR Measurements

	Randomized trial N=888		Registry N=332	P*
Patients, N	PCI+MT=447	MT=441	with FU=166	
FFR significant stenoses - no. per patient	1.5±0.8	1.4±0.7	0.0±0.2	<0.001
No of vessels with ≥ 1 significant stenoses (by FFR) - (%)				
1	74	78	3.0	
2	23	19	0	
3	3	3	0	
Prox- or mid- LAD stenoses - (%)	62	59	0	<0.001
Lesions with FFR ≤ 0.80 - (%)	76	76	2 **	<0.001
Mean FFR in stenoses with FFR ≤ 0.80	0.64±0.13	0.64±0.14	(NA)**	

** Chronic occlusions in the registry patients were arbitrarily assigned an FFR value of 0.50. These patients also had another lesion >50% with an FFR >0.80.

FAME 2 FFR Measurements

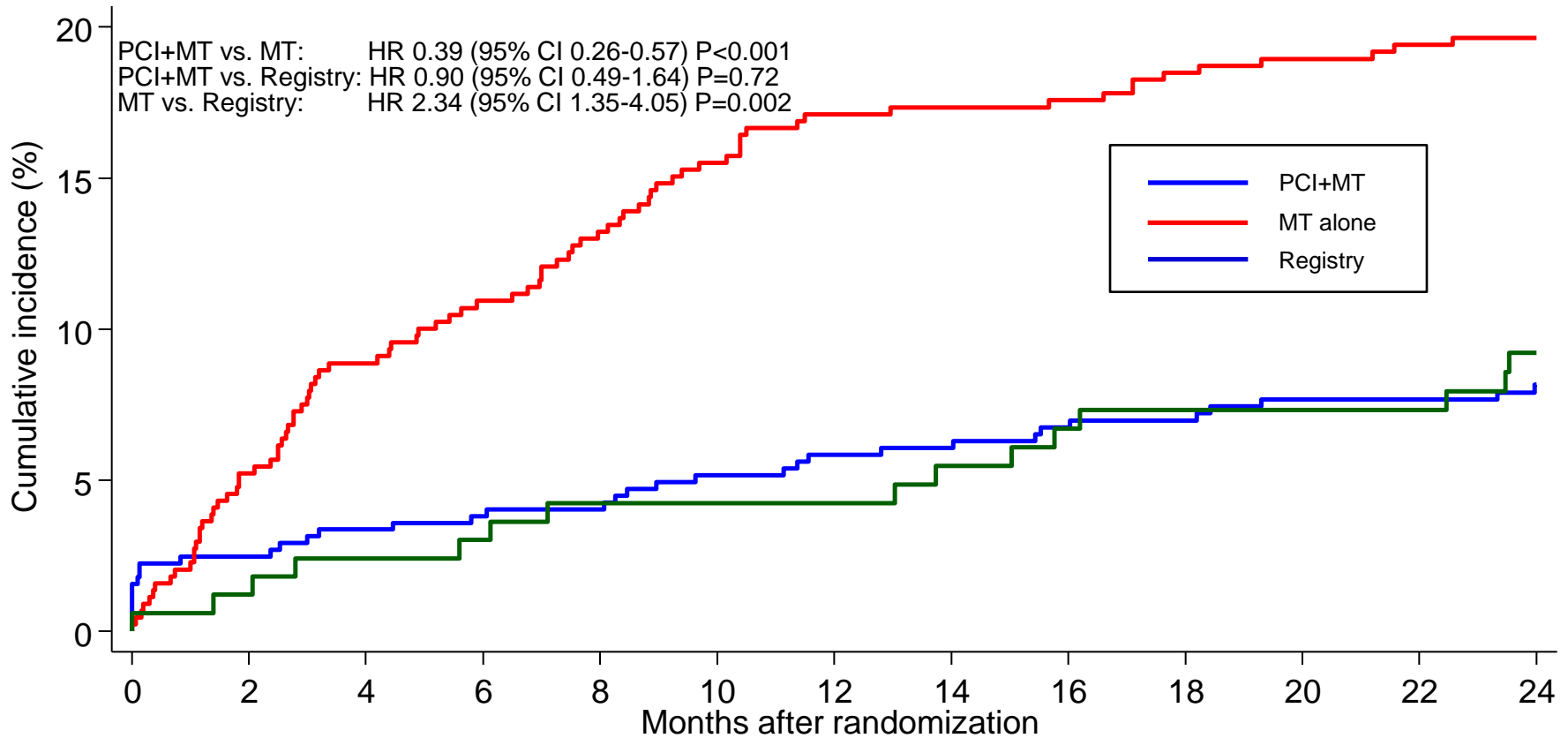
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FAME 2

Results

FAME 2 Primary Outcomes

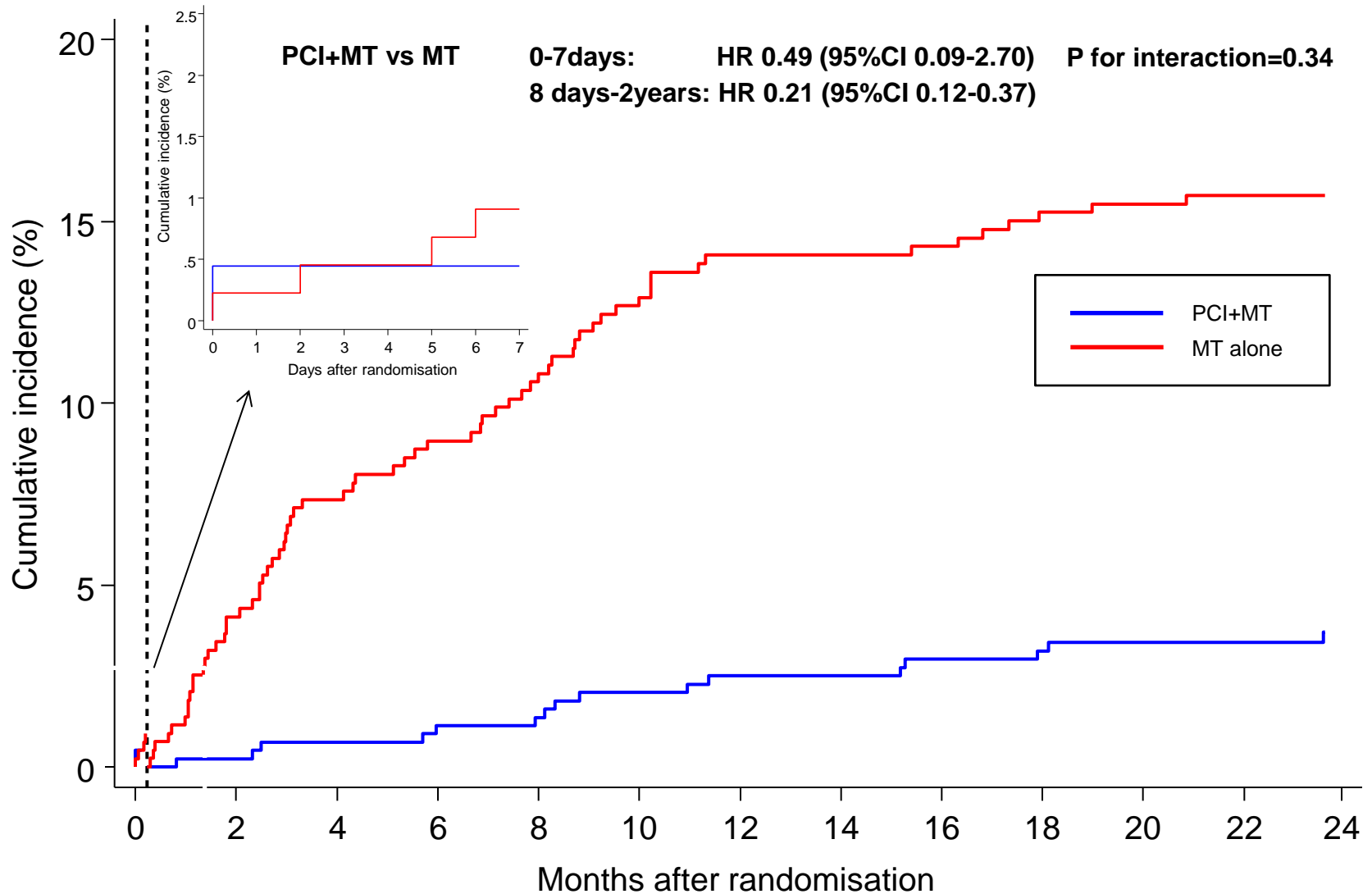


No. at risk

MT	441	417	398	389	379	369	362	360	359	355	353	351	297
PCI+MT	447	434	429	426	425	420	416	414	410	408	405	403	344
Registry	166	164	162	160	157	157	156	153	151	150	150	150	122

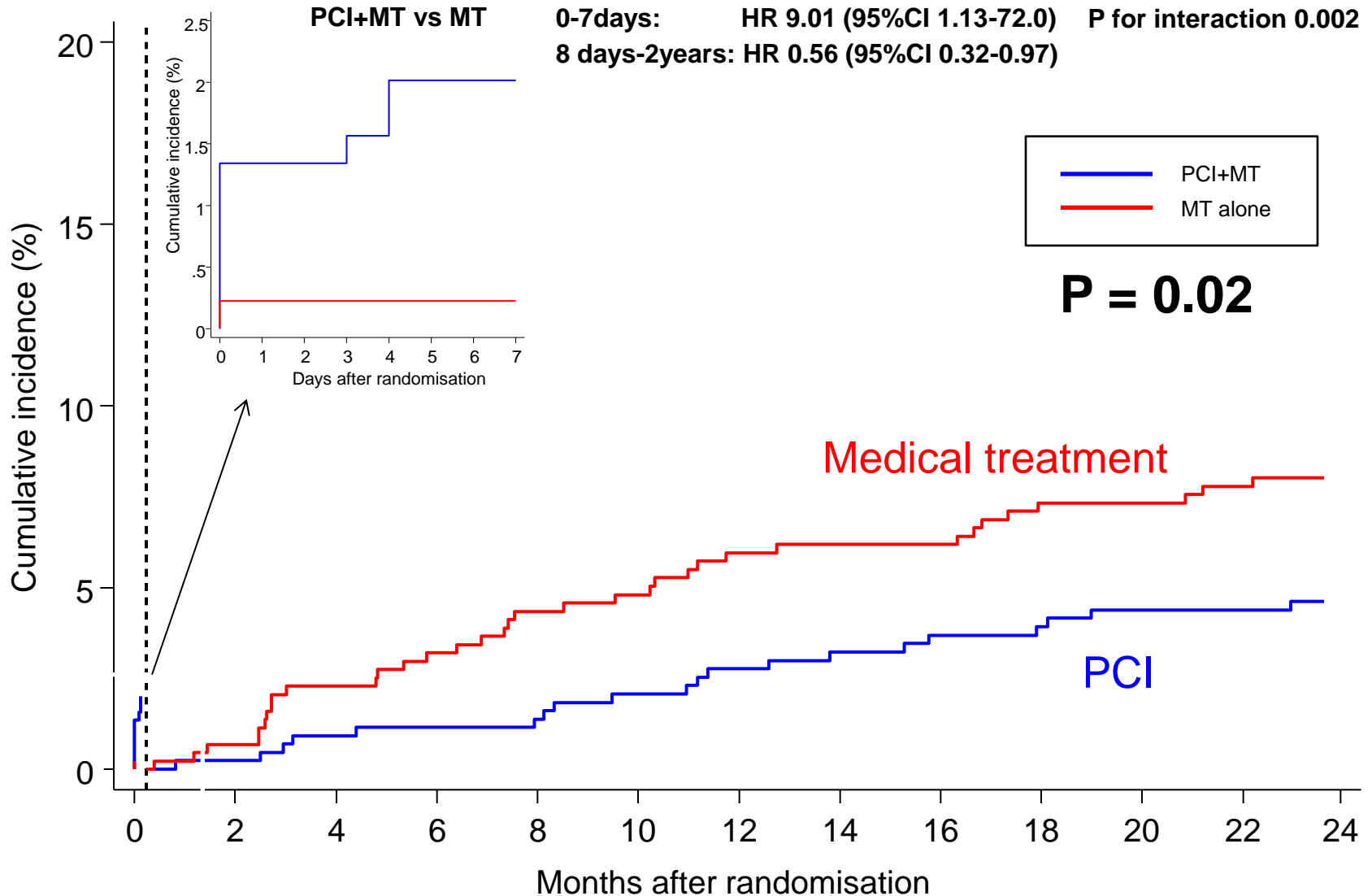
FAME 2

Landmark Analysis for Urgent Revascularization



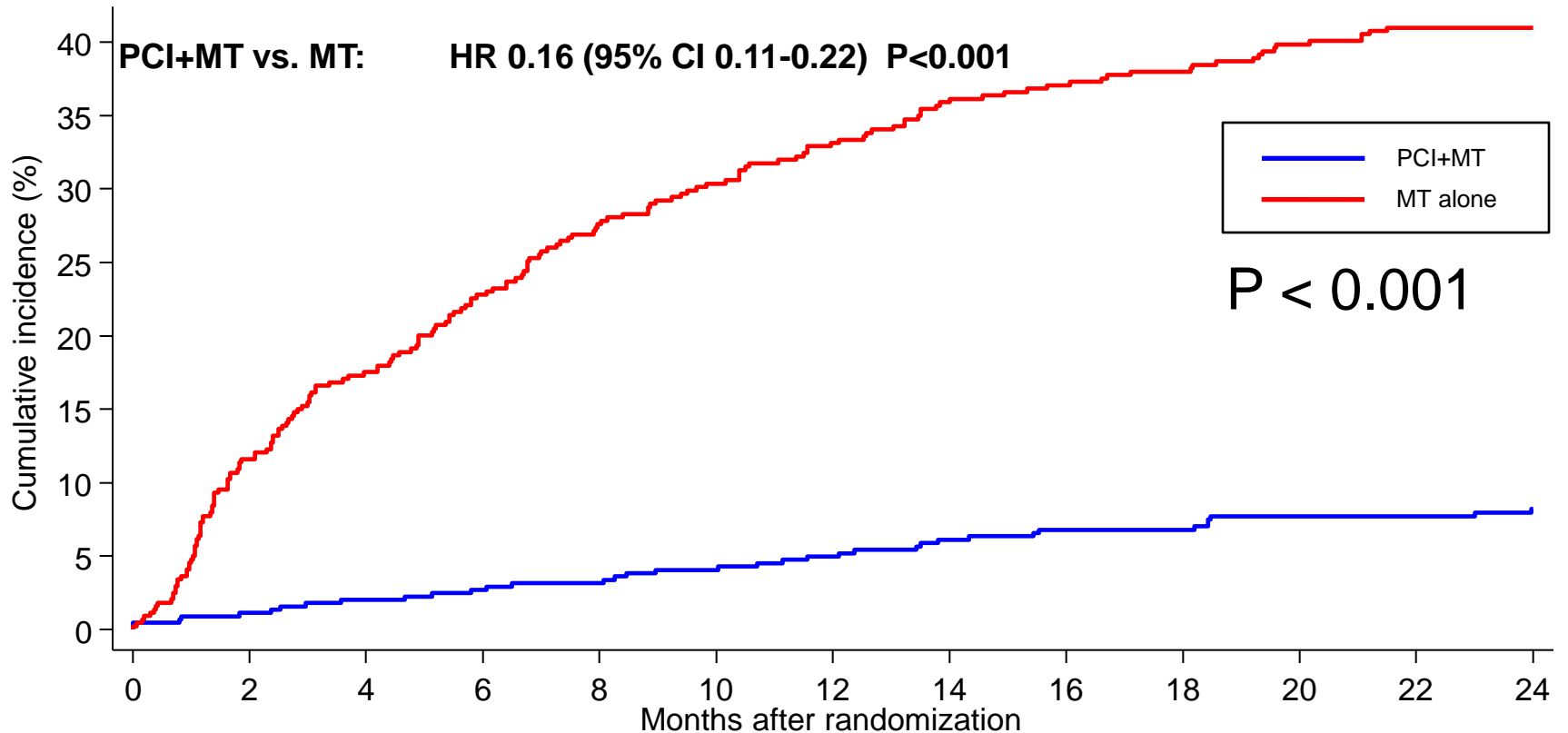
FAME 2

Landmark Analysis for Death or Myocardial Infarction



FAME 2

Urgent AND Non-Urgent Revascularizations



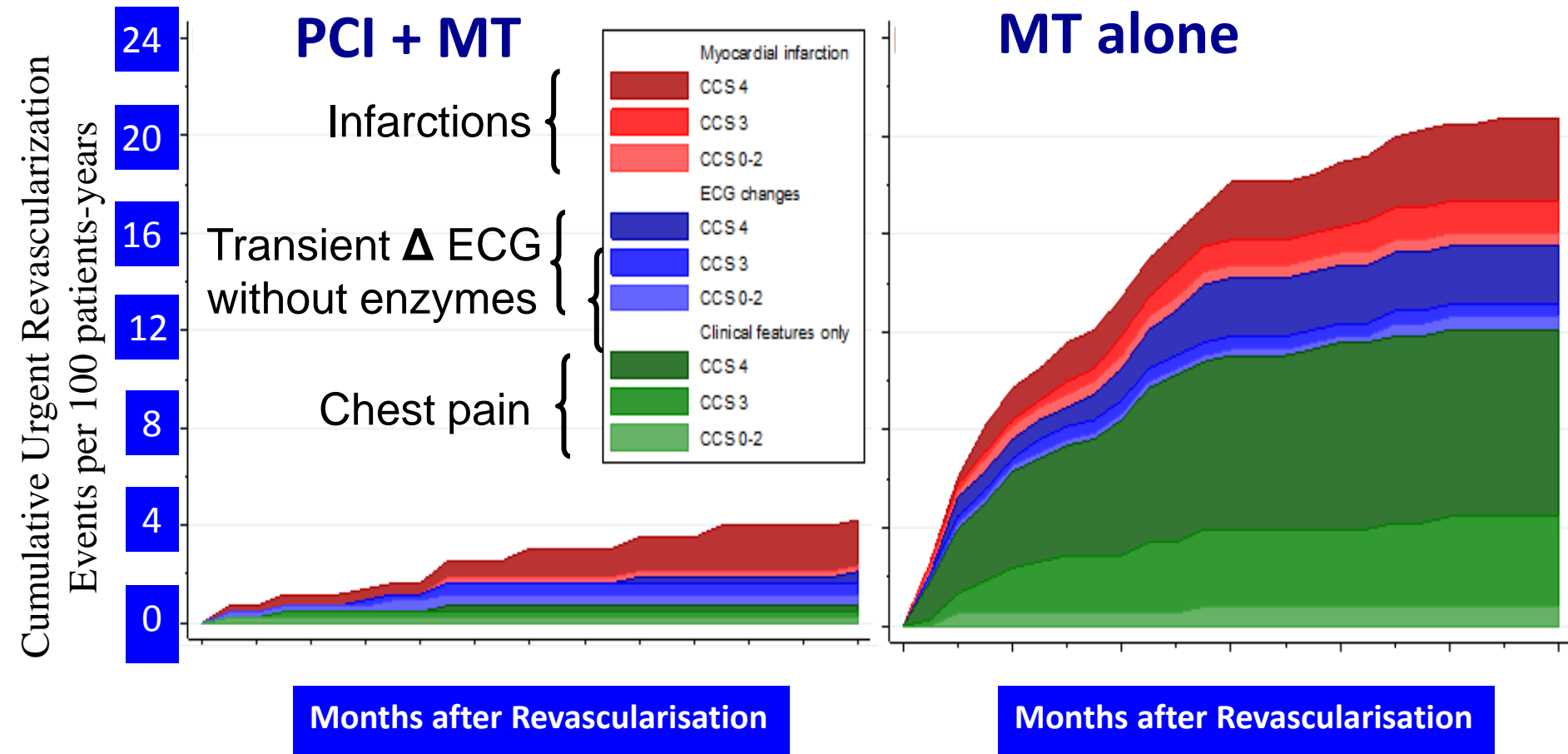
No. at risk

MT	441	389	360	337	315	302	290	277	272	268	260	254	218
PCI+MT	447	440	434	429	427	422	417	410	407	406	402	399	343

After 2 years, > 40% of patients treated by MT had crossed over i.e. had undergone any revascularisation

FAME 2

Urgent revascularizations according to different triggers for the revascularization

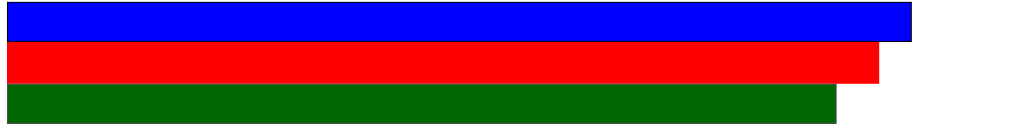


Urgent revascularization was triggered in >80% by an MI, by dynamic ST changes, or by resting angina

FAME 2 Symptoms

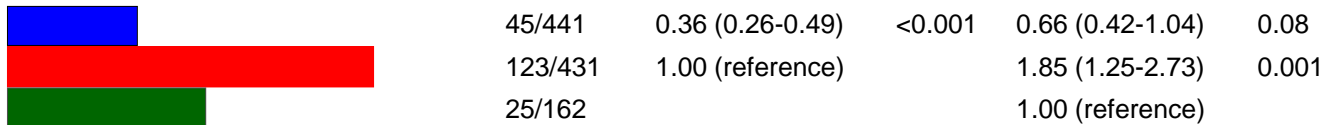
Baseline

PCI+MT
MT alone
Registry



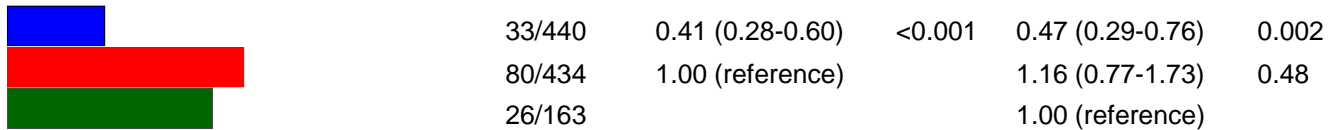
30 Days

PCI+MT
MT alone
Registry



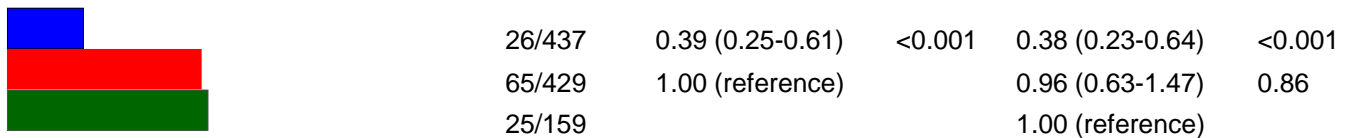
6 Months

PCI+MT
MT alone
Registry



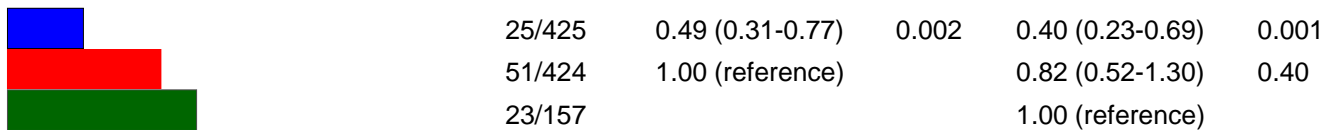
12 Months

PCI+MT
MT alone
Registry



24 Months

PCI+MT
MT alone
Registry



0 20 40 80
Patients with CCS II to IV (%)

FAME 2 : Summary

- 1. The rate of death, MI, or urgent revascularization at 2 years in patients with stable CAD treated with *FFR-guided PCI with new generation drug-eluting stents* was less than half than in patients treated with MT alone.**
- 2. Beyond 7 days from randomization, *FFR-guided PCI significantly reduces the rate of death or MI when compared to MT alone.***
- 3. More than 25% of stable CAD patients scheduled for PCI on the basis of clinical and angiographic data, have no stenosis with an $FFR < 0.80$. These patients have a favorable outcome with MT alone.**



FAME 2 Conclusion

In Patients With Stable Coronary Artery Disease, FFR-guided PCI Improves Outcome as Compared With Medical Treatment Alone

ORIGINAL ARTICLE

Fractional Flow Reserve–Guided PCI for Stable Coronary Artery Disease

Bernard De Bruyne, M.D., Ph.D., William F. Fearon, M.D., Nico H.J. Pijls, M.D., Ph.D., Emanuele Barbato, M.D., Ph.D., Pim Tonino, M.D., Ph.D., Zsolt Piroth, M.D., Nikola Jagic, M.D., Sven Mobius-Winckler, M.D., Gilles Rioufol, M.D., Ph.D., Nils Witt, M.D., Ph.D., Petr Kala, M.D., Philip McCarthy, M.D., Thomas Engström, M.D., Keith Oldroyd, M.D., Kreton Mavromatis, M.D., Ganesh Manoharan, M.D., Peter Verlee, M.D., Ole Frobert, M.D., Nick Curzen, B.M., Ph.D., Jane B. Johnson, R.N., B.S.N., Andreas Limacher, Ph.D., Eveline Nüesch, Ph.D., and Peter Juni, M.D., for the FAME 2 Trial Investigators*

ABSTRACT

BACKGROUND

We hypothesized that in patients with stable coronary artery disease and stenosis, percutaneous coronary intervention (PCI) performed on the basis of the fractional flow reserve (FFR) would be superior to medical therapy.

METHODS

In 1220 patients with stable coronary artery disease, we assessed the FFR in all stenoses that were visible on angiography. Patients who had at least one stenosis with an FFR of 0.80 or less were randomly assigned to undergo FFR-guided PCI plus medical therapy or to receive medical therapy alone. Patients in whom all stenoses had an FFR of more than 0.80 received medical therapy alone and were included in a registry. The primary end point was a composite of death from any cause, nonfatal myocardial infarction, or urgent revascularization within 2 years.

RESULTS

The rate of the primary end point was significantly lower in the PCI group than in the medical-therapy group (8.1% vs. 19.5%; hazard ratio, 0.39; 95% confidence interval [CI], 0.26 to 0.57; $P<0.001$). This reduction was driven by a lower rate of urgent revascularization in the PCI group (4.0% vs. 16.3%; hazard ratio, 0.23; 95% CI, 0.14 to 0.38; $P<0.001$), with no significant between-group differences in the rates of death and myocardial infarction. Urgent revascularizations that were triggered by myocardial infarction or ischemic changes on electrocardiography were less frequent in the PCI group (3.4% vs. 7.0%, $P=0.01$). In a landmark analysis, the rate of death or myocardial infarction from 8 days to 2 years was lower in the PCI group than in the medical-therapy group (1.8% vs. 6.0%, $P=0.004$). Among registry patients, the rate of the primary end point was 9.0% at 2 years.

CONCLUSIONS

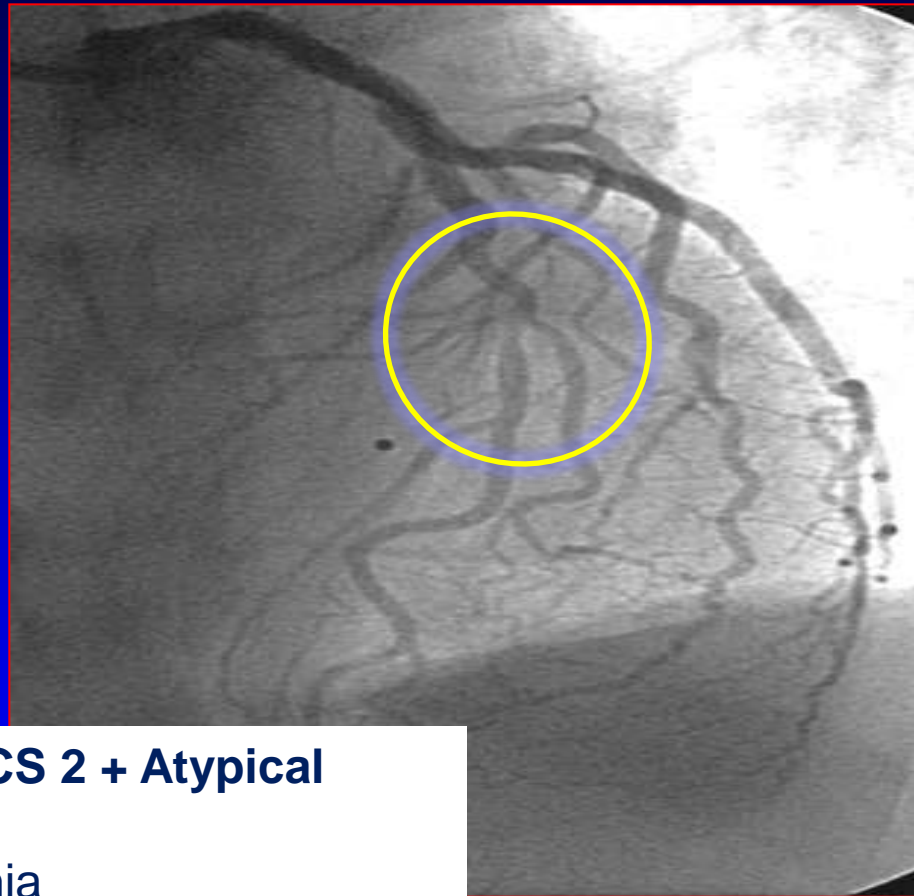
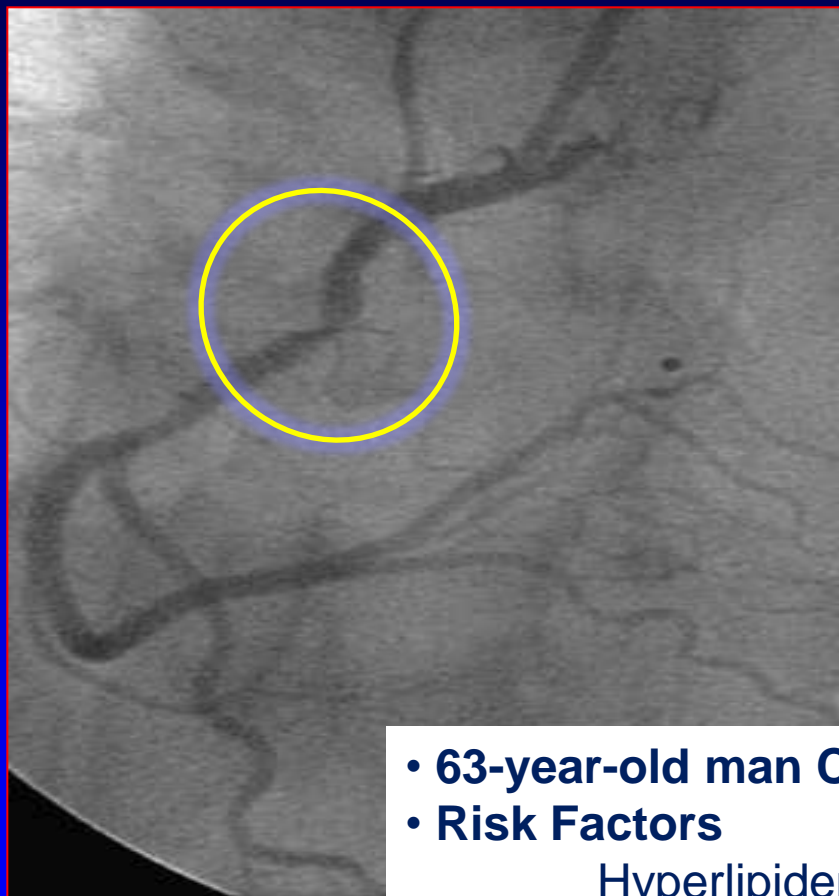
In patients with stable coronary artery disease, FFR-guided PCI, as compared with medical therapy alone, improved the outcome. Patients without ischemia had a favorable outcome with medical therapy alone. (Funded by St. Jude Medical; FAME 2 ClinicalTrials.gov number, NCT01132495.)

New Engl J Medic 2012;367:991-1001

New Engl J Medic 2014;371:online ahead of print

FAME 2 Illustrative Cases

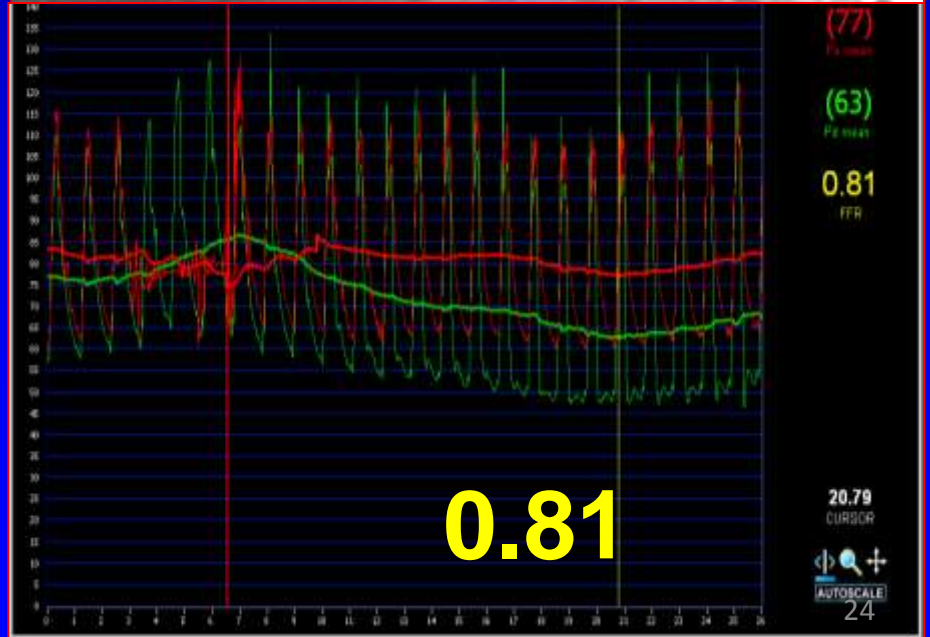
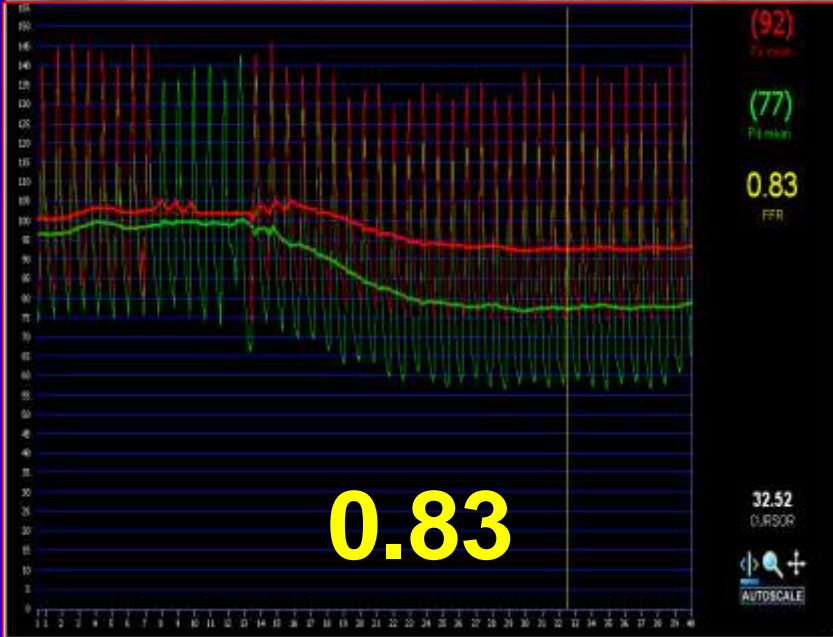
Case 2



- **63-year-old man CCS 2 + Atypical**
- **Risk Factors**
 - Hyperlipidemia
 - Arterial hypertension
 - Diabetes Type II
- **Coronary CT angio: “severe” stenoses**
- **Abnormal exercise ECG**

FAME 2 Illustrative Cases

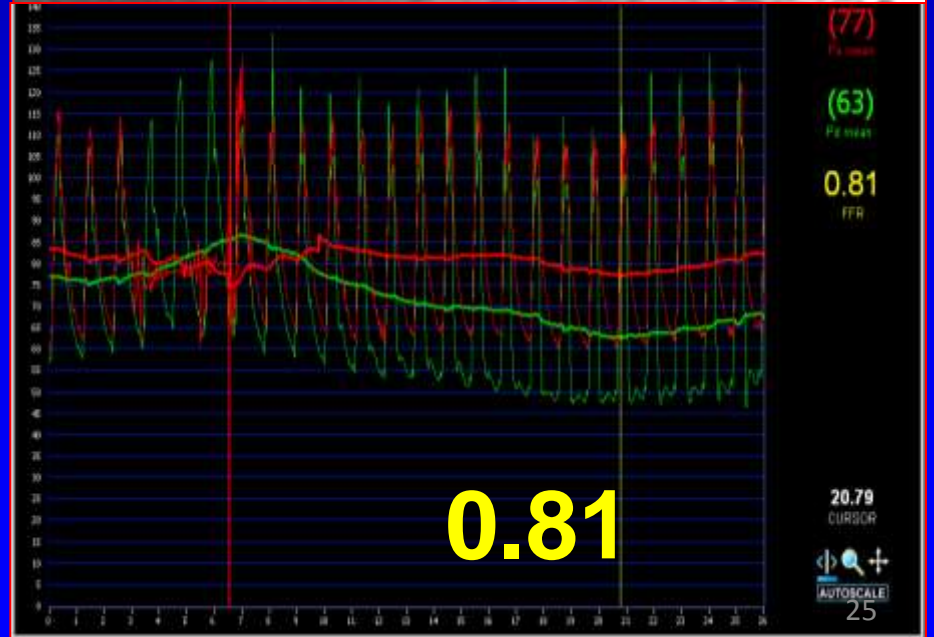
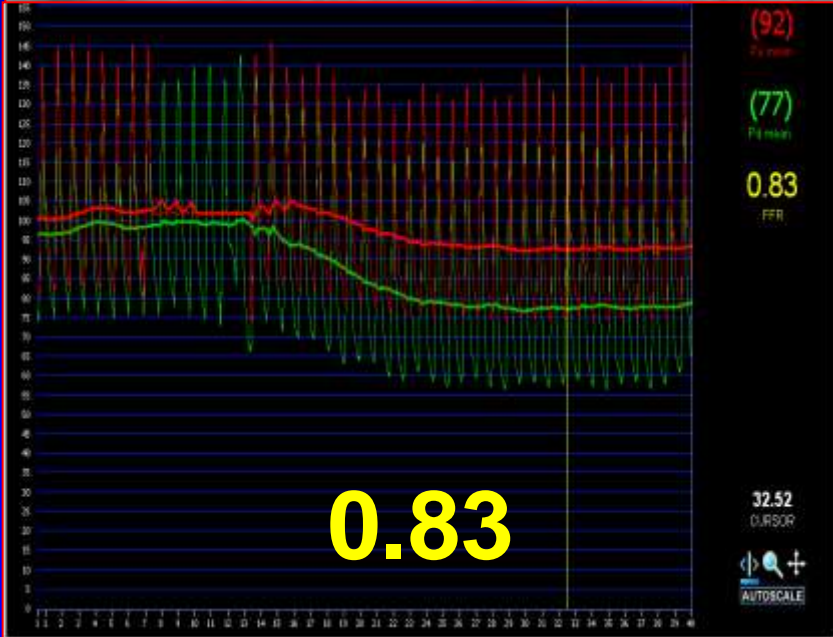
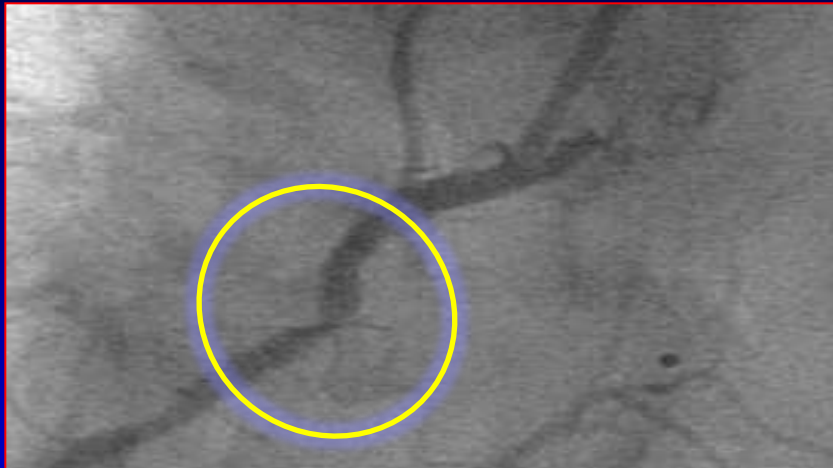
Case 2



FAME 2 Illustrative Cases

Case 2

→ *registry*



EINDE

FAME 2 Baseline Clinical Characteristics (2)

	Randomized trial N=888		Registry N=332	P*
Patients, N	PCI+MT=447	MT=441	with FU=166	
Non-Cardiac Co-Morbidity				
Renal Failure (Cr > 2.0 mg/dL) - (%)	2	3	3	0.14
History of stroke or TIA - (%)	8	7	6	0.52
Peripheral vascular disease - (%)	10	11	5	0.03
Cardiac History				
History of MI - (%)	38	39	38	0.92
History of PCI in target vessel - (%)	18	17	21	0.36
Angina - (%)				0.60
Asymptomatic	12	10	10	
CCS class I	18	22	25	
CCS class II	46	45	45	

*P value compares all RCT patients with patients in registry

14