



ORIGINAL ARTICLE

Fractional Flow Reserve–Guided PCI for Stable Coronary Artery Disease

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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 (4.6% vs. 8.0%, $P=0.04$). 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.)

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*A complete list of investigators and committee members in the Fractional Flow Reserve versus Angiography for Multivessel Evaluation 2 (FAME 2) trial is provided in the Supplementary Appendix, available at NEJM.org.

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FAME 2

Report of the Primary Endpoint

ClinicalTrials.gov NCT01132495

Potential conflicts of interest

Speaker's name: Bernard De Bruyne

☐ **I have the following** potential conflicts of interest to report:

- ☒ Research contracts
- ☒ Consulting
- ☐ Employment in industry
- ☐ Stockholder of a healthcare company
- ☐ Owner of a healthcare company
- ☐ Other(s)

☐ **I do not have any potential conflict of interest**

Study Supported by St. Jude Medical

FAME 2 Background

PCI is the preferred treatment in acute coronary syndromes, but has never been shown to reduce 'hard end-points' in stable coronary artery disease.

FAME 2 Objective

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

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 $\text{FFR} \leq 0.80$ (n=888)

Randomization 1:1

PCI + MT

MT

73%

When all $\text{FFR} > 0.80$
(n=332)

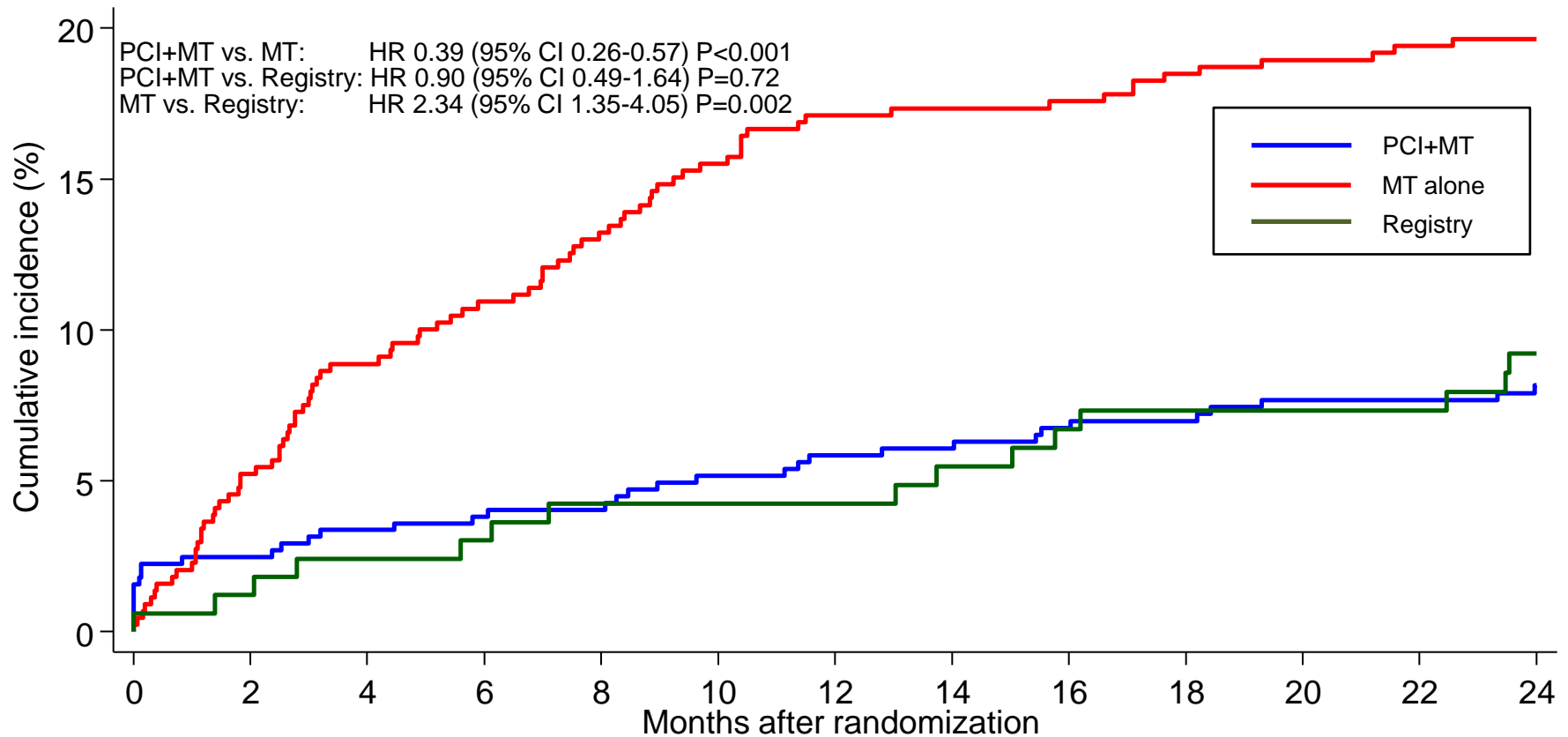
MT

27%

50% randomly
assigned to FU

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

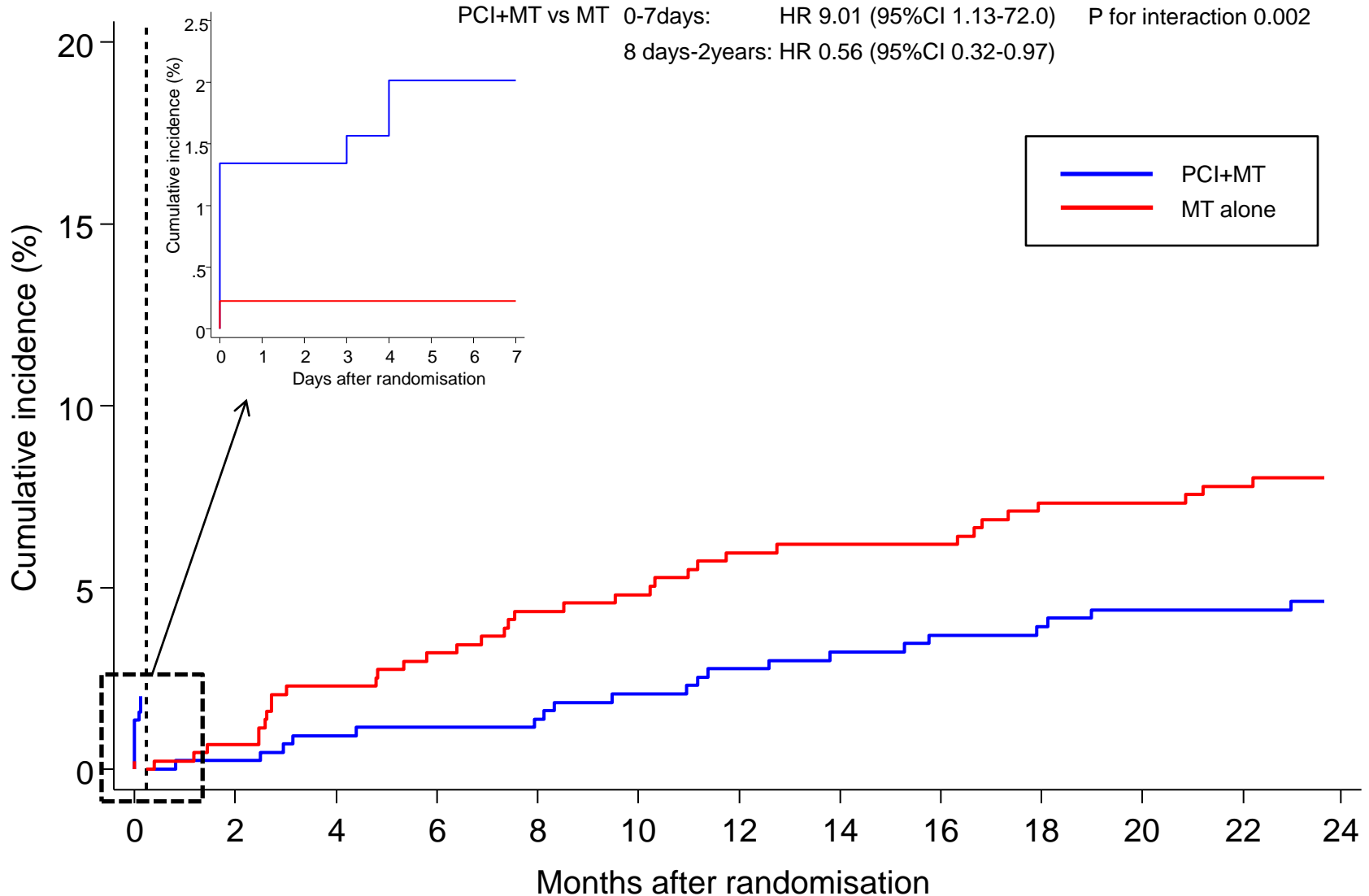
FAME 2 Primary Outcomes



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 Death/Myocardial Infarction Landmark Analysis



FAME 2 Summary

1. The rate of the composite of death, MI, or urgent revascularization at 2 years in patients with stable CAD treated with FFR-guided PCI with new generation DES was less than half than in patient treated with MT alone.
2. Patients in whom the stenoses are not able to induce ischemia ($\text{FFR} > 0.80$) are doing well with MT alone.
3. Beyond 7 days from randomisation, PCI plus MT significantly reduces the rate of death or MI when compared to MT alone.

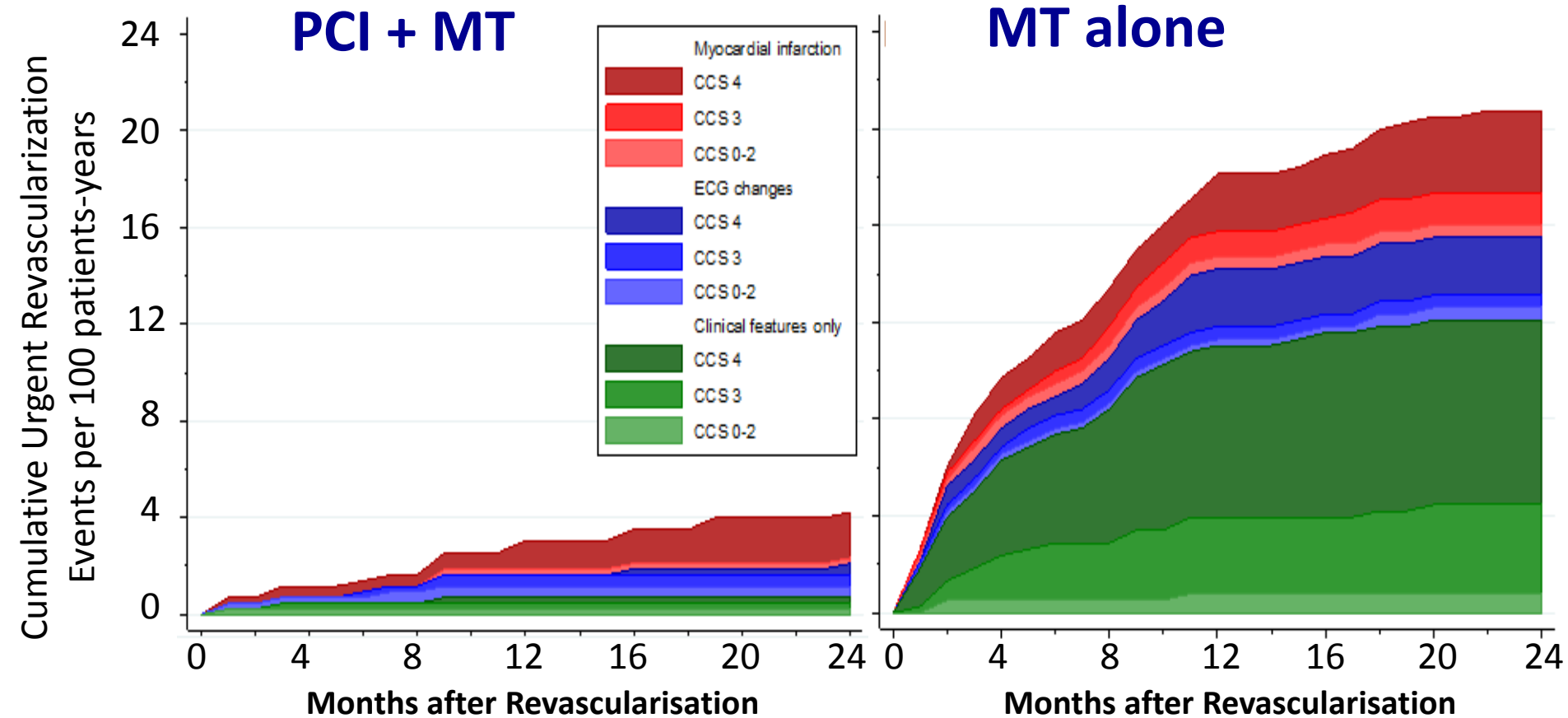
CONCLUSION

In patients with stable CAD, PCI is superior to MT provided

- ✓ FFR is used to guide the procedure
- ✓ DES of 2nd generation are implanted

FAME 2

Urgent revascularisations according to different triggers for the revascularisation

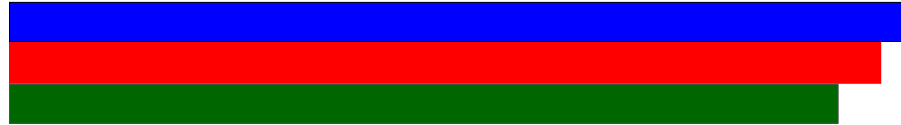


Urgent revascularisation was triggered in > 80% by an MI, by dynamic ST changes, or by resting angina

FAME 2 Symptoms

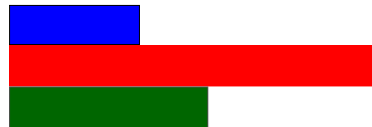
Baseline

PCI+MT
MT alone
Registry



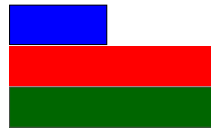
30 Days

PCI+MT
MT alone
Registry



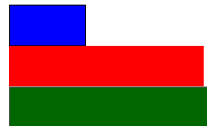
6 Months

PCI+MT
MT alone
Registry



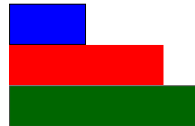
12 Months

PCI+MT
MT alone
Registry



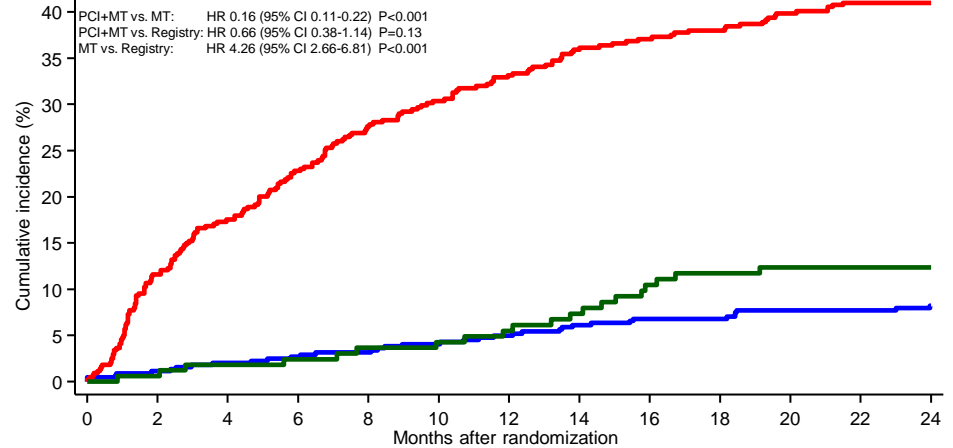
24 Months

PCI+MT
MT alone
Registry



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

Total Revascularisations



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
Registry	166	165	162	160	157	156	153	149	144	142	141	141	116