MR-INFORM

ACC.17
66th Annual Scientific Session & Expo

MR-INFORM: STRESS PERFUSION IMAGING TO GUIDE THE MANAGEMENT OF PATIENTS WITH STABLE CORONARY ARTERY DISEASE

EIKE NAGEL, MD, FACC
UNIVERSITY HOSPITAL FRANKFURT

WASHINGTON, DC
FRI • SAT • SUN
MARCH 17 – 19, 2017

BACKGROUND

- Management of patients with stable coronary artery disease is based on reduction of risk factors, optimal medical therapy (OMT) and revascularization in those with resistant symptoms and proven ischemia.
- Invasive angiography with PCI remains the main management strategy in patients with stable angina despite medication.

MR-INFORM

Optimal invasive strategy

- The FAME and DEFER studies demonstrated convincingly, that adding intracoronary pressure measurements (FFR) to invasive angiography and limiting revascularization to patients with hemodynamically significant stenoses results in a prognostic benefit.
- A combination of OMT with invasive angiography supported by FFR seems the current best **invasive** management strategy for patients with stable angina.

MR-INFORM

Optimal non-invasive strategy

- Non-invasive ischemia testing with perfusion imaging has been shown to accurately predict the presence of a flow limiting stenosis as well as predict outcome.
- Cardiovascular magnetic resonance (MR) perfusion imaging has demonstrated the highest accuracy of non-invasive testing without requiring radiation as well as gaining significant information on anatomy, function and myocardial structure in a single session.
- A combination of OMT with MR-perfusion imaging seems the current best **non-invasive** management strategy for patients with stable angina.

MR-INFORM

Hypothesis

Guiding the initial management of patients with stable angina and intermediate to high risk of coronary artery disease receiving OMT by MR-perfusion imaging is non-inferior to invasive angiography supported by FFR.

MR-INFORM

Trial Structure

Sponsor: Guy's and St. Thomas' Hospital and King's College London, UK
Funding: Biomedical Research Centre (National Institute of Health Research, UK), German Centre for Cardiovascular Research (DZHK) and Bayer Healthcare, Germany (unrestricted grant)
CRO: pharmtrace, Berlin, Germany

- 9 UK Sites
  - King's College London and Guy's and St. Thomas' Hospital, London
  - King's College Hospital, London
  - Heart Hospital, London
  - Leeds General Infirmary, Leeds
  - Glenfield General Hospital, Leicester
  - Golden Jubilee National Hospital Glasgow
  - Bristol Heart Institute, Bristol
  - Freeman Hospital, Newcastle
  - Royal Brompton & Harefield Hospitals
- Portugal
  - Gaia Hospital, Porto
- 5 Germany
  - Elisabeth Hospital, Essen
  - Heart Centre Leipzig, Leipzig
  - University Hospital Heidelberg
  - Robert-Bosch-Hospital, Stuttgart
  - Helios Clinics Berlin-Buch, Berlin
- Australia
  - Flinders Medical Centre, Adelaide

Inclusion criteria

- Stable angina (CCS II-III)

  and

- either ≥2 risk factors (smoking, diabetes, hypertension, hyperlipidemia, pos family hx)

  or

- positive exercise treadmill test

Exclusion criteria

- Contraindication to MR or adenosine
- Atrial fibrillation or frequent ectopic beats
- EF < 30%
- CCS class IV
- NYHA class III or IV
- Previous CABG
- PCI within the previous 6 months
- eGFR < 30 mL/min/1.73m^2
- Disability to lie supine for 60 minutes
- Medically unstable
- Pregnant, breast feeding, unable/unwilling to consent

MR-INFORM

Randomization (1:1)

FFR INFORMED

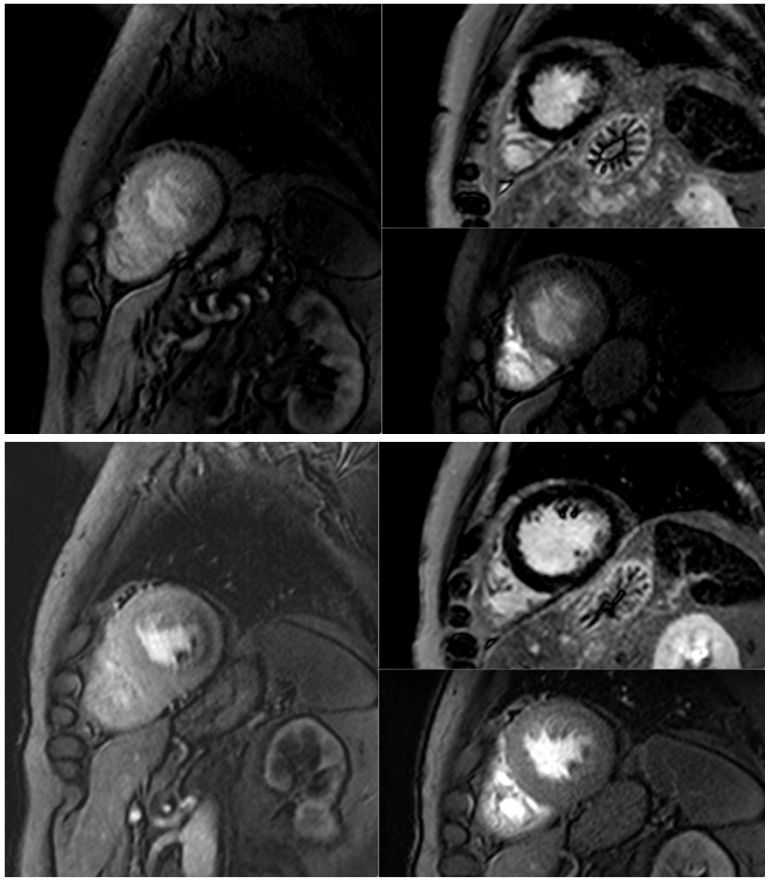
- Invasive angiography in all patients
- FFR in all arteries >2.5 mm with a stenosis of 40-95%
- If FFR <0.8 revascularization (PCI or CABG) recommended
- CTO regarded as positive

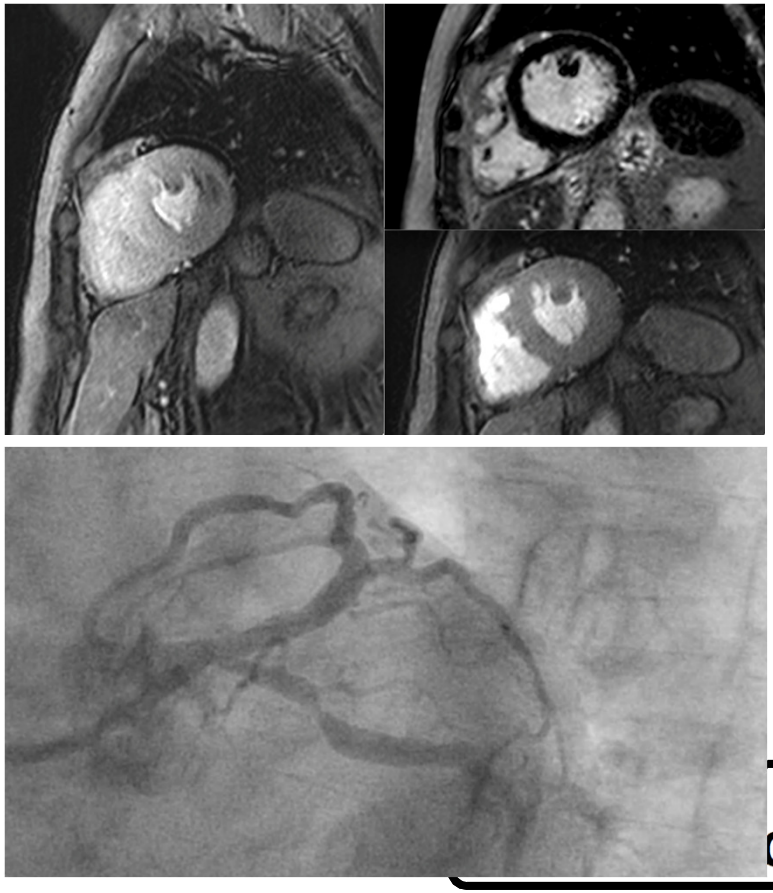
MR INFORMED

- 1.5T multivendor
- Cine imaging
- Adenosine stress/rest first pass perfusion imaging using 0.075 mmol Gadovist / kg body weight for first pass
- Late gadolinium enhancement after top-up to 0.2 mmol/kg body weight
- If transmural defect or subendocardial defect >2 segments or in 2 adjacent slices was found, angiography with aim of revascularization recommended

MR-INFORM

Example, 67 y, male, CCS II, 2 RF





ORM

Optimal Medical Therapy (OMT)

All patients received OMT:

- Advice to all patients and their primary physicians
- Aspirin or clopidogrel
- Statin
- ACE inhibitor or ARB

Targets:

- Total cholesterol < 4 mmol/l
- LDL < 2 mmol/l
- BP ≤ 130/80 mmHg
- Random glucose < 6 mmol/l
- BMI < 25
- No smoking

MR-INFORM

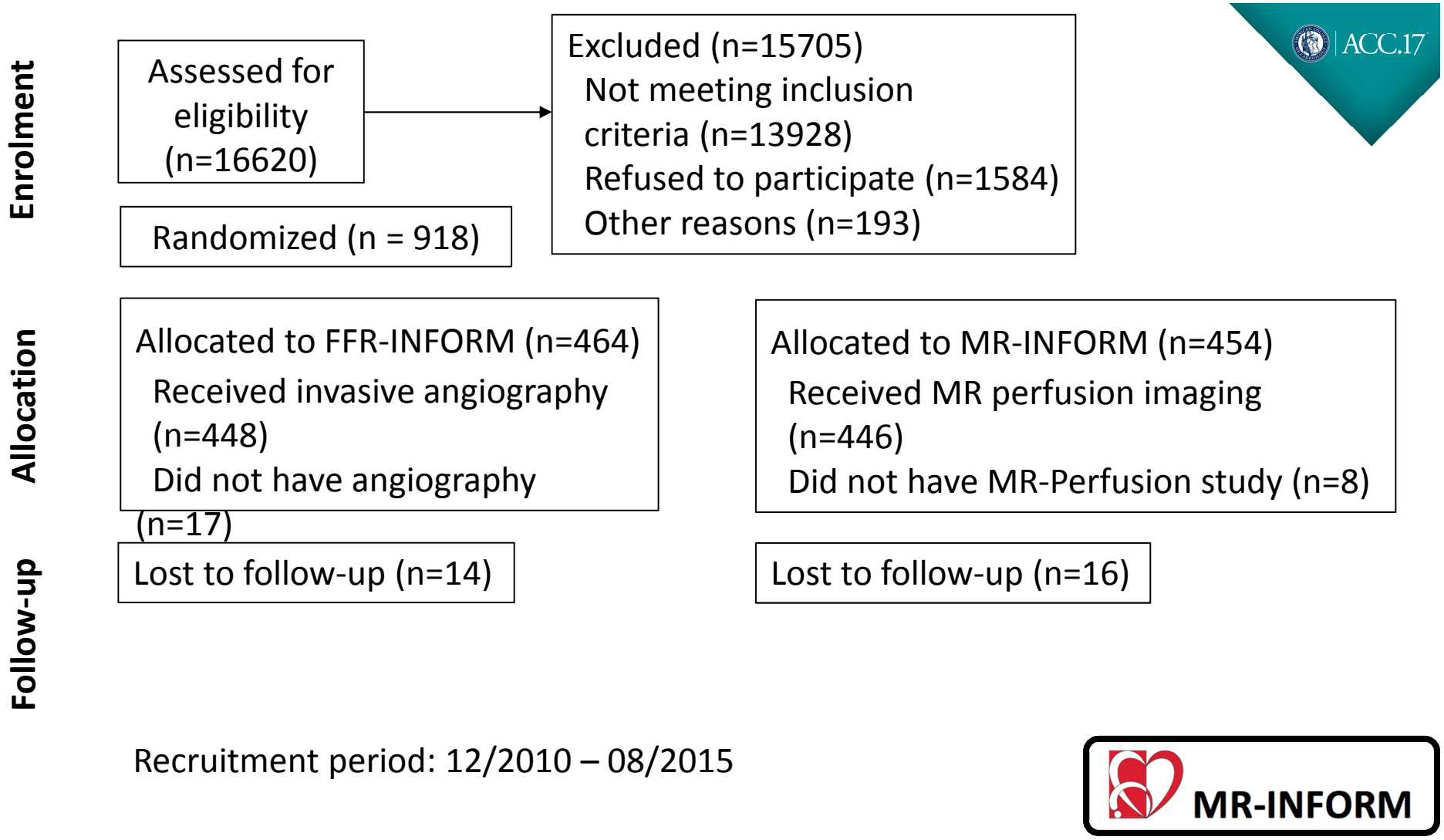
Primary Endpoint

Composite endpoint of

- All cause mortality
- Nonfatal myocardial infarction (clinical presentation of ACS AND Q-waves OR troponin ≥99th percentile)
- Re-revascularization of a vessel targeted at the index revascularization procedure

Power Calculation

- An incidence of 10% and an equivalence margin of 10% were assumed
- 826 patients required to determine non-inferiority of an MR guided strategy compared to an FFR guided strategy with a power of 80% and a $p<0.025$.
- Allowing for a drop-out rate of 10% a total sample size of 918 was required.



Recruitment period: 12/2010 – 08/2015

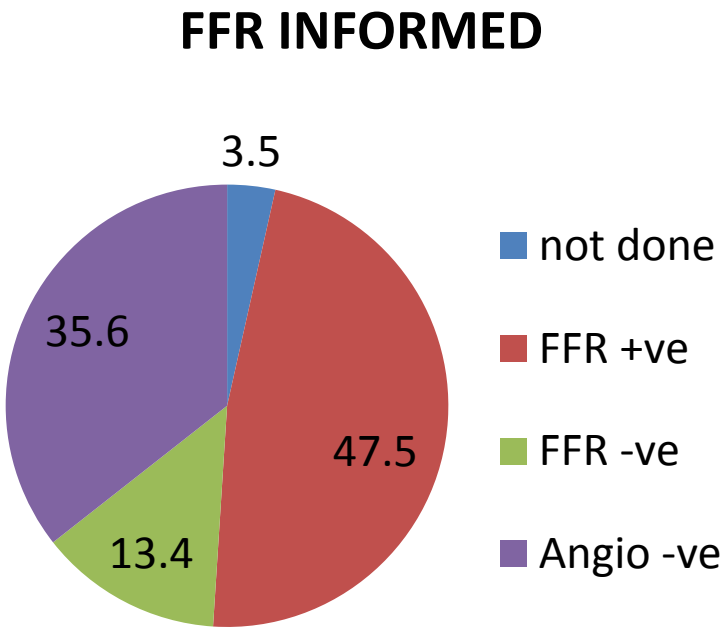
ACC.17

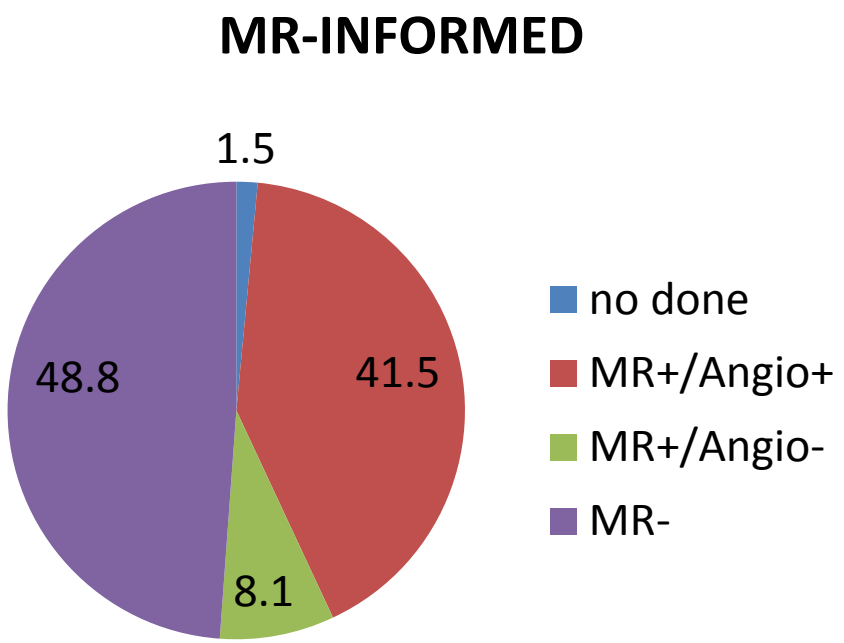
MR-INFORM

Patient characteristics

	FFR-INFORMED (n=464)	MR-INFORMED (n=454)
Age	61.6 ± 9.37	62.4 ± 9.61
Gender (Male)	329 (72.47%)	335 (72.20%)
Ejection Fraction	58.9 ± 7.88	61.2 ± 7.12
Ethnicity (Caucasian)	419 (90.69%)	409 (89.89%)
CCS class II III	415 (89.63%) 48 (10.37%)	407 (90.04%) 45 (9.96%)
Diabetes	138 (29.74%)	112 (24.72%)
Previous Myocardial Infarction	33 (7.11%)	39 (8.61%)
Known CAD	52 (11.21%)	72 (15.89%)
Current Smoking	76 (16.38%)	82 (18.06%)

Results of the index test

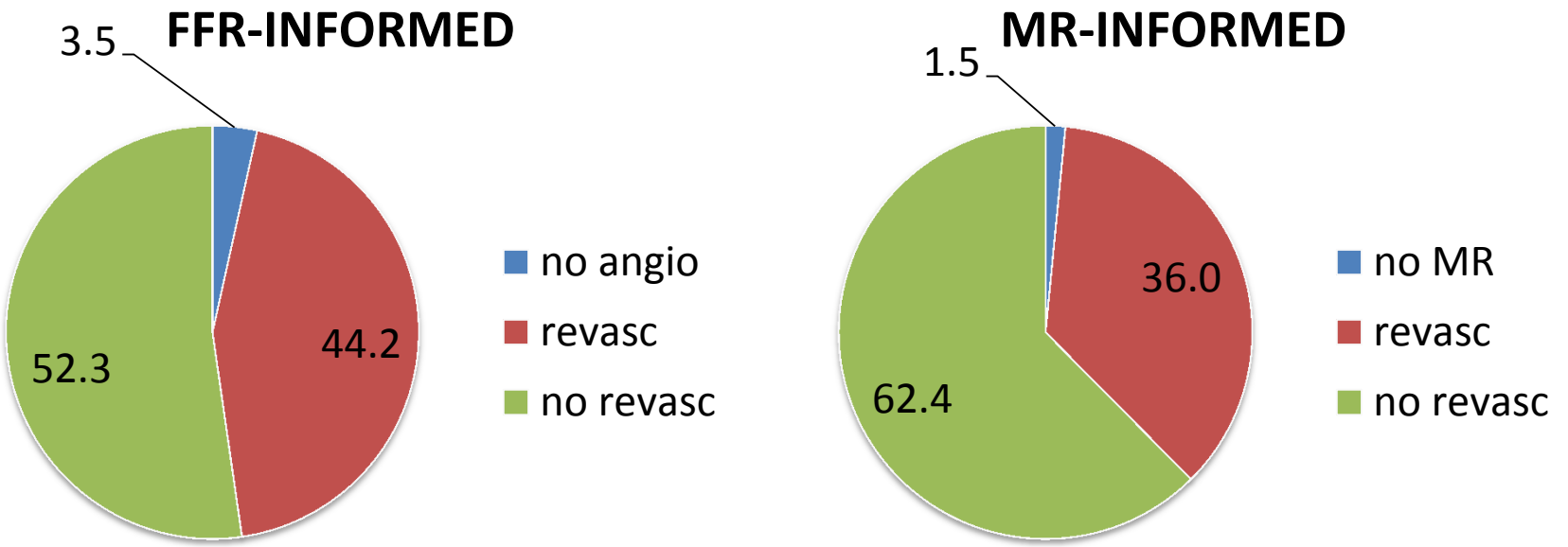




Significant CAD by positive anatomical AND functional test
p = 0.0047

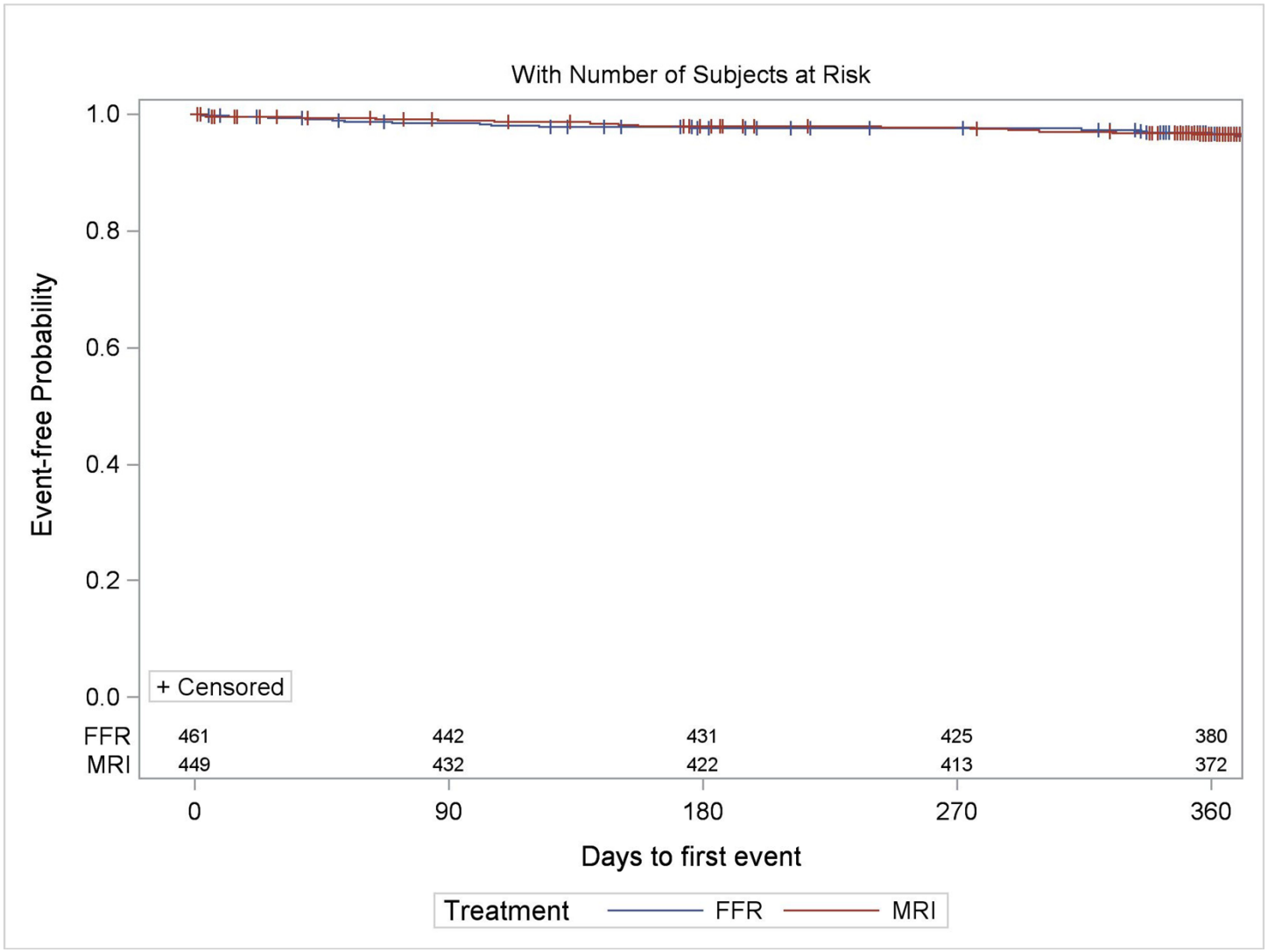
MR-INFORM

Revascularization rate



Revascularization rate
p = 0.0053

MR-INFORM



ACC.17

FFR

MR

MR-INFORM

MACE

	FFR (n = 462)	MR (n = 450)
Events (n)	18 (3.9%)	15 (3.33%)
• Death	1 (Angio +, CABG planned, death before CABG)	4 (2 non-cardiac, 1 MR+, Angio+, CABG planned, death before CABG 1 death after CABG)
• Myocardial Infarction	8	8
• Re-revascularization	9	3
Absolute Risk Difference [95% CI]	-0.56 [-2.98; 1.86]	
Hazard ratio [95% CI]	-0.852 [-0.43; 1.69]; p = 0.62	

MR-INFORM

Discussion / Summary

- Guiding the initial management of patients with stable angina and an intermediate to high risk for coronary artery disease with non-invasive MR-perfusion imaging is non-inferior to a strategy with invasive angiography supported by FFR during a follow-up of one year.
- Both strategies are safe and result in a low total event rate.
- The number of revascularization procedures is significantly lower when guided by MR perfusion imaging in comparison to invasive angiography supported by FFR.

MR-INFORM

Investigators

- Eike Nagel
- John Greenwood
- Gerry McCann
- Nuno Bettencourt
- Ajay Shah
- Shazzia Hussain
- Divaka Perera
- Sven Plein
- Chiara Bucciarelli-Ducci
- Matthias Paul
- Mark Westwood
- Michael Marber
- Wolf-Stefan Richter
- Valentina Puntmann
- Carsten Schwenke
- Jeanette Schulz-Menger
- Rajiv Das
- Joyce Wong
- Derek Hausenloy
- Henning Steen
- Colin Berry

On behalf of the MR-INFORM Investigators

- Matt Sydes (DMC)
- Mark Norell (DMC)
- Jamil Mayet (DMC)
- Theo Karamitsos (DMC)
- Simon Redwood
- Wolfgang Utz
- Holger Thiele
- Oliver Bruder
- Heiko Mahrholdt
- Khaled Alfakih
- Phil McCarthy
- Reza Razavi
- Gregorius Korosoglou
- Sebastian Buss
- Matthias Friedrich
- Matthias Gutberlet
- Georg Fürnau
- Joseph Selvanayagam

MR-INFORM