COMPARE-ACUTE

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Randomised trial of FFR-guided complete revascularization *versus* infarct artery only treatment in multivessel STEMI patients

On behalf of all COMPARE-ACUTE investigators

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Compare Acute

MAASSTAD ZIEKENHUIS

COMPARE-ACUTE is an investigator initiated, multicenter, prospective randomized trial

The Netherlands
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Haga Ziekenhuis, Den Haag
Atrium Medisch Centrum, Heerlen
Rijnstate Ziekenhuis, Arnhem
Universitair Medisch Centrum, Groningen
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Trial Organization

Steering committee
Pieter Smits (PI), Gert Richardt, Mohamed Abdel-Wahab, Elmir Omerovic, Franz-Josef Neumann

DSMB
Per-Anders Jansson, Marianne Hartford, Kjell Petersson

CRO
Gothia Forum (Gothenburg, Sweden): monitoring, data management
Diagram (Zwolle, The Netherlands): core lab and clinical event adjudication

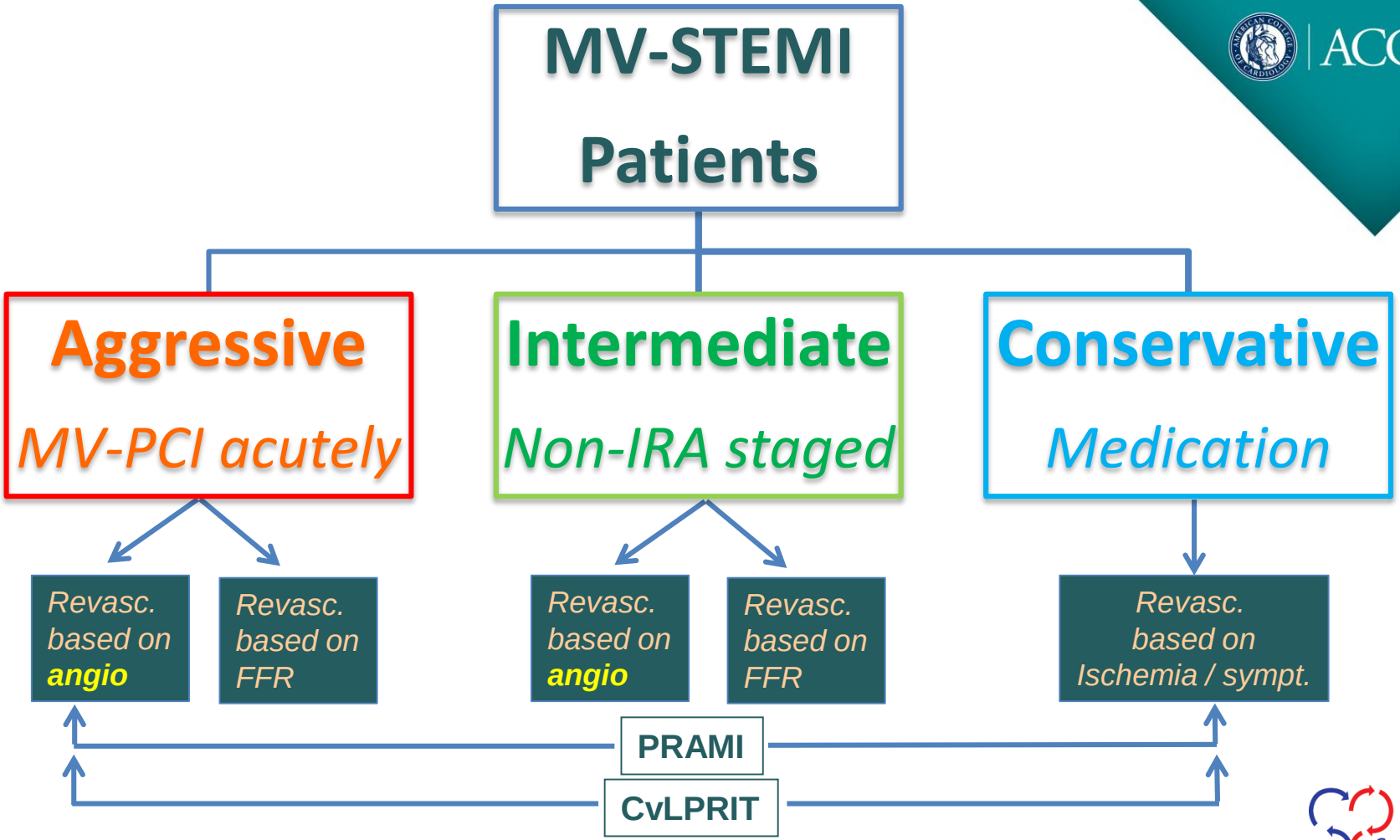
Statistic analysis
Bianca Boxma - de Klerk

Sponsor
Maasstad Cardiovascular Research Organisation (Rotterdam, The Netherlands), receiving research grants from Abbott Vascular and St. Jude Medical

Introduction

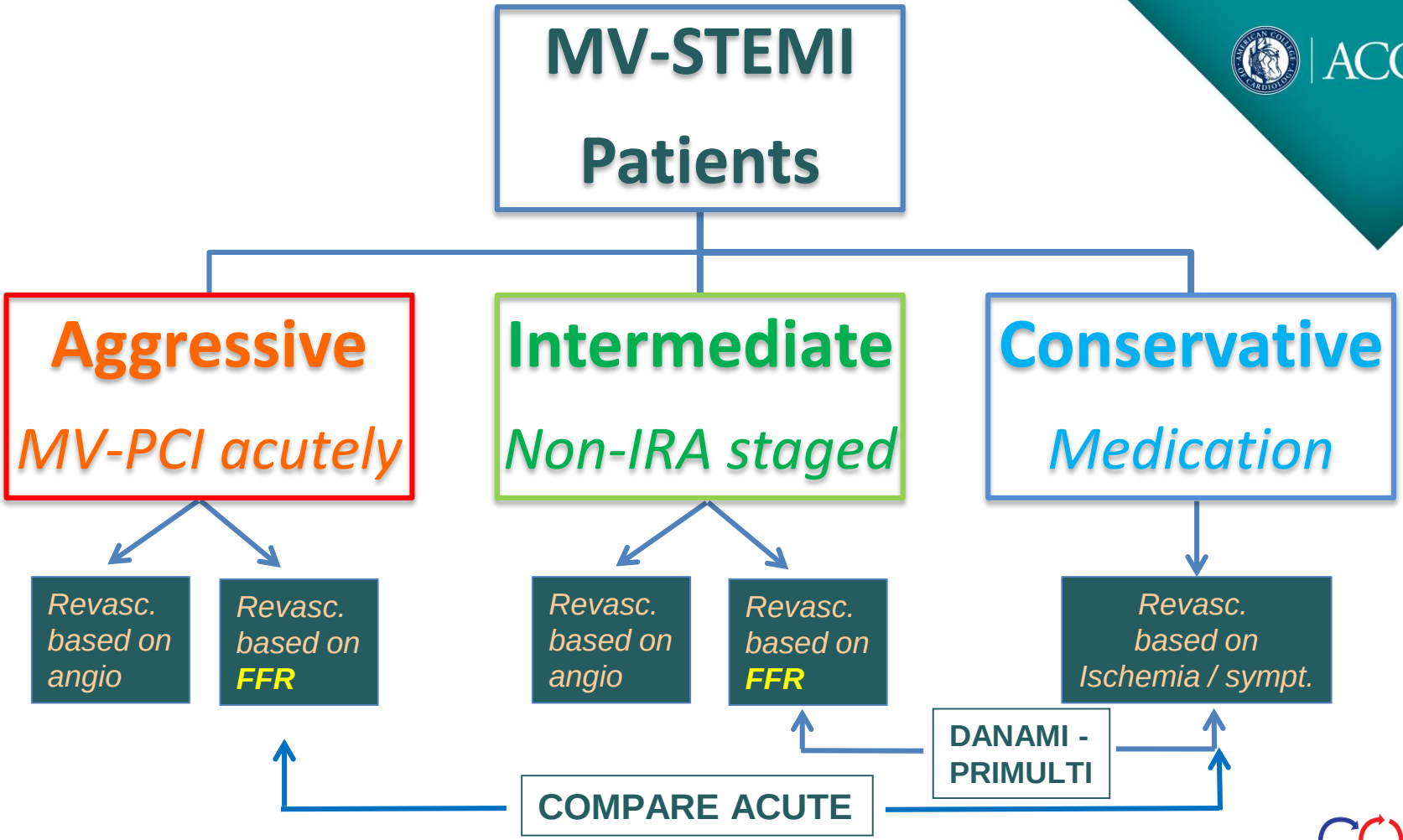
- Approximately 50% of the STEMI patients have multivessel disease at presentation; meaning 50% or more diameter stenosis in one or more non-infarct-related arteries (non-IRAs)

- What and when to do with these non-infarct-related artery (non-IRA) lesions remains a unresolved clinical dilemma



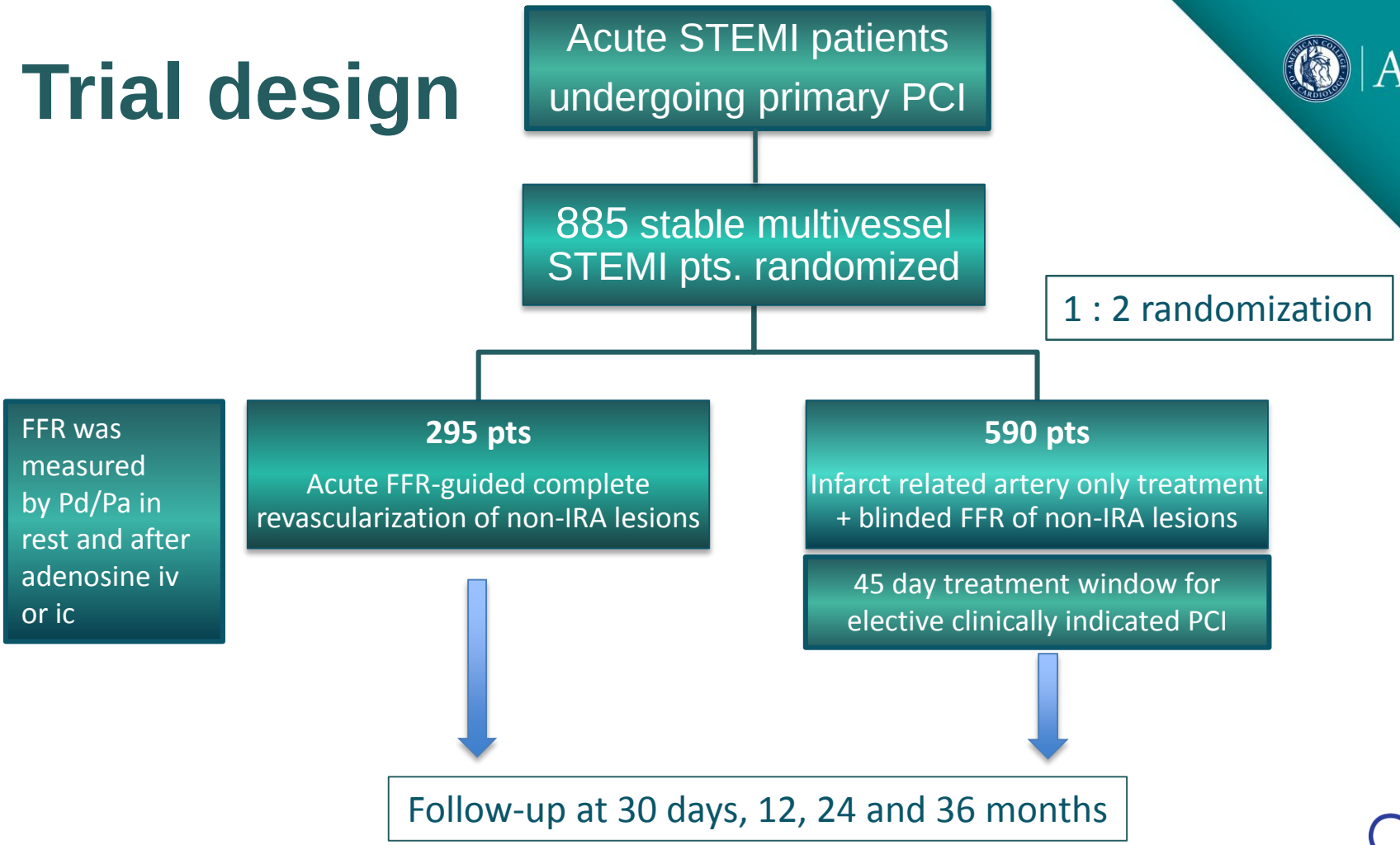
PRAMI: Wald et al. NEJM 2013; 369: 1115-23

CvLPRIT: Gerschlick et al. JACC 2015; 65: 963-72



DANAMI-3-PRIMULTI: Engstrom et al. Lancet 2015; 386: 665-71

Trial design



Key In- and Exclusion Criteria

Inclusion Criteria

- Pts. between18-85 years old
- Presenting with STEMI within 12 hours of onset of complaints with an indication for primary PCI
- And of which the non-IRAs - or their major side branches of ≥2.0 mm in diameter - demonstrated lesions with ≥50% stenosis by quantitative coronary angiography (QCA) or visual assessment and were judged feasible for PCI by the operator

Exclusion Criteria

- Left main disease
- Chronic total occlusion or severe stenosis with TIMI flow ≤ II of the non-IRA lesion
- Suboptimal result or complications after treatment of IRA
- Severe valve dysfunction
- Killip Class III or IV

Endpoints

Primary endpoint:

The composite of all-cause death, recurrent myocardial infarction, recurrent revascularization and cerebrovascular event (MACCE) at 12 months follow-up

Secondary endpoints:

- The primary endoint (MACCE) at 24 and 36 months
- The components of the primary endpoint at 12, 24 and 36 months
- The composite of all-cause death and myocardial infarction at 12, 24 and 36 months
- The composite of cardiac death, myocardial infarction, revascularization, cerebrovascular event and major bleeding (NACE) at 12, 24 and 36 months
- Major bleeding at 48 hours and 12 months
- Stent thrombosis at 12, 24 and 36 months
- Treatment costs at 12, 24 and 26 months

Endpoint adjudication

- All events were independently monitored and adjudicated
- Recurrent revascularizations were adjudicated for indication (clinically indicated or not) and setting (urgent or elective)
- Clinically indicated revascularization was defined as:
  1. Stenosis of ≥50% by QCA and one of the following: recurrent angina pectoris, ischemic ECG changes, ischemic non-invasive or invasive test findings, all presumably related to the target vessel
  2. Stenosis of ≥70% by QCA, without objective signs of angina or ischemia
- Elective, clinically indicated revascularizations performed within 45 days after the primary PCI procedure in the IRA only group were not counted as an event

Baseline characteristics

	FFR guided Complete Revascularization (n=295)	Infarct Artery Only Revascularization (n=590)	p-value
Mean age (sd) - yr	62 (10)	61 (10)	0.22
Male – no. (%)	233 (79.0%)	450 (76.3%)	0.37
Medical history – no. %			
Diabetes	43 (14.6%)	94 (15.9%)	0.60
Hypertension	136 (46.1%)	282 (47.8%)	0.63
Current Smoker	120 (40.8%)	287 (48.7%)	**0.03**
Hypercholesterolemie	95 (32.2%)	176 (29.8%)	0.47
Family history of premature CAD	103 (35.0%)	223 (37.8%)	0.42
Previous Stroke	10 (3.4%)	26 (4.4%)	0.47
Prevous MI	22 (7.5%)	48 (8.1%)	0.73
Previous PCI	25 (8.5%)	44 (7.5%)	0.60
Renal impairment *	3 (1.0%)	7 (1.2%)	0.82
Peripheral vessel disease	10 (3.4%)	23 (3.9%)	0.71

* A creatinine value of more than 133 µmol/l or patients in dialysis

Baseline characteristics

	FFR guided Complete Revascularization (n=295)	Infarct Artery Only Revascularization (n=590)	p-value
Location of infarct - no. (%)†			
Posterior MI	53 (18.0%)	96 (16.3%)	0.53
Anterior MI	105 (35.6%)	206 (34.9%)	0.84
Inferior MI	149 (50.5%)	307 (52.0%)	0.67
Lateral MI	41 (13.9%)	86 (14.6%)	0.79
Impossible to determine	3 (1.0%)	4 (0.7%)	0.59
Primary PCI within 6 / 6-12 / >12 hours of onset symptoms - no.(%)	<6h: 225 (76.3%) 6-12h: 47 (15.9%) >12h: 23 (7.8%)	<6h: 462 (78.3%) 6-12h: 84 (14.2%) >12h: 44 (7.5%)	0.58
Arteries with stenosis –no. (%)			
2	204 (69.2%)	396 (67.1%)	0.54
3	91 (30.8%)	194 (32.9%)	
Killip class ≥2 – no. (%)	15 (5.1%)	30 (5.1%)	1.00
Median maximum CK (range) – IU/l	1040 (102-8182)	1125 (112-11052)	0.62

† The location of the infarct was determined on the basis of electrocardiography

Procedural data: infarct artery lesions

	FFR guided Complete Revascularization (295 pts, 327 lesions)	Infarct Artery Only Revascularization (590 pts, 645 lesions)	p-value
Mean IRA lesions per patient	1.11 ± 0.35	1.10 ± 0.33	0.32
Mean ref.vessel diameter IRA - mm	3.1 ± 0.5	3.2 ± 0.5	0.08
Mean IRA lesions length – mm	21.1 ± 12.1	22.3 ± 13.1	0.15
RCA – no. (%) LAD – no. (%) RCX – no. (%) LM – no. (%)	147 (45.0%) 110 (33.6%) 69 (21.1%) 1 (0.3%)	296 (45.9%) 233 (36.1%) 115 (17.8%) 1 (0.2%)	0.25
Pre-procedure TIMI flow (0-3) – no. (%)	0: 172 (52.6%) 1: 25 (7.6%) 2: 63 (19.3%) 3.:67 (20.5%)	0: 364 (56.4%) 1: 57 (8.8%) 2: 109 (16.9%) 3:115 (17.8%)	0.16
ACC/AHA Classification – no. (%)	A: 35 (10.7%) B1: 69 (21.1%) B2: 112 (34.3%) C:111 (33.9%)	A: 73 (11.3%) B1: 148 (22.9%) B2:189 (29.3%) C: 235 (36.4%)	0.93
Treatment (DES) – no. (%)	312 (95.4%)	620 (96.1%)	0.62

Procedural data: non-infarct artery lesions

	FFR guided Complete Revascularization (295 pts, 451 non-IRA lesions)	Infarct Artery Only Revascularization (590 pts, 856 non-IRA lesions)	p-value
Mean non-IRA lesions per patient	1.54 ± 0.81	1.56 ± 0.85	0.91
RCA – no. (%) LAD – no. (%) RCX – no. (%) LM – no. (%)	118 (26.2%) 184 (40.8%) 149 (33.0%) 0 (0.0%)	206 (24.1%) 360 (42.1%) 290 (33.9%) 0 (0.0%)	0.71
Pre-procedure TIMI flow (0-3) – no. (%)	0: NA 1: NA 2: 9 (2.0%) 3: 441 (98.0%)	0: 5 (0.6%) 1: 4 (0.5%) 2: 10 (1.2%) 3: 831 (97.3%)	0.19
ACC/AHA Classification – no. (%)	A: 102 (26.0%) B1: 124 (31.7%) B2: 93 (23.8%) C: 72 (18.4%)	NA	NA
Treatment (DES) – no. (%)	209 /216 (96.8%)	NA	NA

Compare Acute

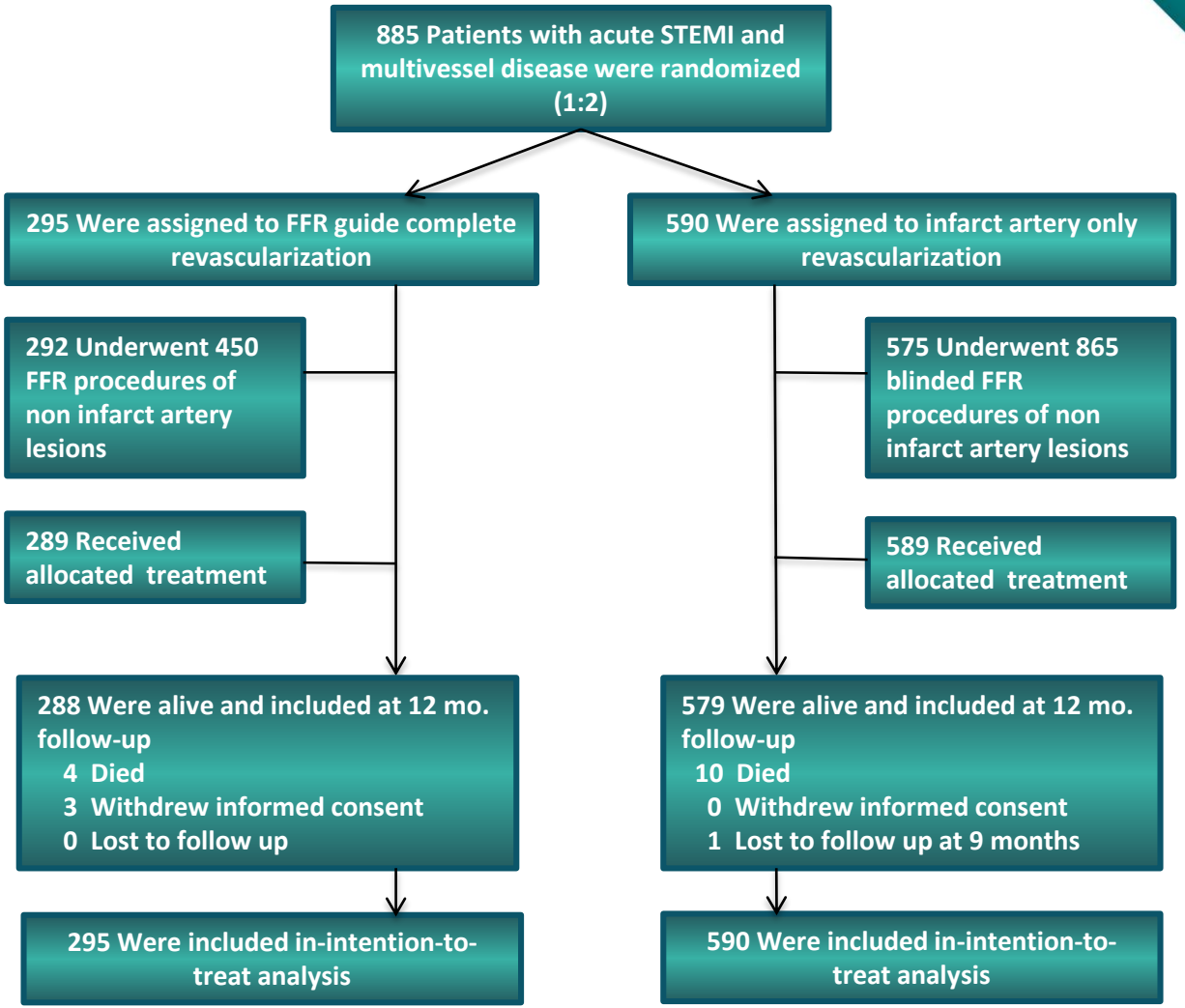
Procedural data

	FFR guided complete Revascularization (295 pts.)	Infarct Artery Only Revascularization (590 pts.)	p-value
Pts. with treated (FFR guided) non-IRA lesions – no.(%) during index PCI procedure delayed during index hospitalization	163 (55.3%)¶ 136 (83.4%) 27 (16.6%)§	NA	
Mean index procedure time – min	65 ± 31	59 ± 28	**0.001**
Mean contrast volume during index PCI procedure – ml	224 ± 104	202 ± 75	**0.007**
Median (range) hospital stay - days	4 (1 – 35)	4 (1 -71)	0.36
Pre-discharge non-invasive stress tests – no.(%)	21 (7.1%)	71 (12.0%)	**0.03**

¶ 158 pts. FFR guided + 5 pts without FFR guidance underwent non-IRA treatment

§ mean delay of 2.1 ± 1.0 days

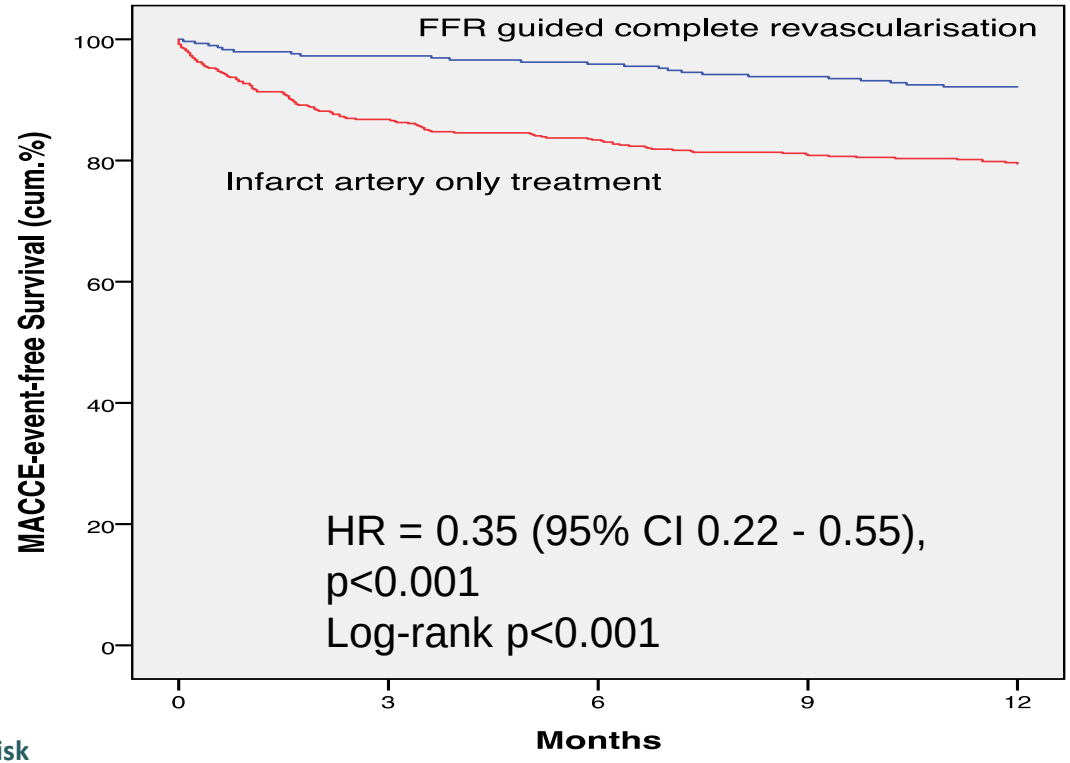
Compare Acute


885 Patients with acute STEMI and multivessel disease were randomized (1:2)
295 Were assigned to FFR guide complete revascularization
590 Were assigned to infarct artery only revascularization
292 Underwent 450 FFR procedures of non infarct artery lesions
289 Received allocated treatment
575 Underwent 865 blinded FFR procedures of non infarct artery lesions
589 Received allocated treatment
288 Were alive and included at 12 mo. follow-up
4 Died
3 Withdrew informed consent
0 Lost to follow up
579 Were alive and included at 12 mo. follow-up
10 Died
0 Withdrew informed consent
1 Lost to follow up at 9 months
295 Were included in-intention-to-treat analysis
590 Were included in-intention-to-treat analysis

FFR outcome

	FFR-guided Complete n=295 pts (450 lesions)	IRA-only n=590 pts (856 lesions)	P value
FFR measurements	292 (99.0%)	575 (97.5%)	0.13
Min. FFR (mean ± SD)	0.78 ± 0.12	0.79 ± 0.12	0.42
Positive FFR value (≤ 0.80)	158/292 (54.1%)	275/575 (47.9%)	0.08
Negative FFR value (>0.80)	134/292 (45.9 %)	300/575 (52.1%)	

Primary outcome



7.8%

20.5%

No. at risk					
FFR guided complete	295	286	281	264	215
Culprit lesion only	590	512	492	457	371

Primary outcome and its components

* MACCE = the composite of all-cause mortality, non-fatal myocardial infarction, any revascularization and cerebrovascular events.

	FFR guided Complete Revascularization (n=295)	Infarct Artery Only treatment (n=590)	HR	95% CI	P value
Primary endpoint	Number of events (%)				
MACCE* (any first event)	23 (7.8%)	121 (20.5%)	0.35	0.22 – 0.55	**<0.001**
Death, all cause	4 (1.3%)	10 (1.7%)	0.80	0.25 – 2.56	0.70
Cardiac	3 (1.0%)	6 (1.0%)			
Myocardial infarction (MI)	7 (2.4%)	28 (4.7%)	0.50	0.22 - 1.13	0.10
Spontaneous	5 (1.6%)	17 (2.9%)	0.59	0.22 – 1.59	0.29
Peri-procedural	2 (0.6%)	11 (1.9%)	0.36	0.08 – 1.64	0.19
Revascularization	18 (6.1%)	103 (17.5%)	0.32	0.20 – 0.54	**<0.001**
PCI	15 (5.1%)	98 (16.6%)	0.37	0.24 – 0.57	**<0.001**
CABG	3 (1.0%)	5 (0.8%)	1.20	0.29 – 5.02	0.80
Cerebrovascular event	0 (0.0%)	4 (0.7%)	NA	NA	NA

Secondary endpoints

** NACE = Net Adverse Clinical Events; the composite of cardiac death, myocardial Infarction, any revascularization, stroke and major bleeding.

	FFR guided Complete Revascularization (n=295)	Infarct Artery Only treatment (n=590)	HR	95% CI	P value
Secondary endpoints	Number of events (%)				
NACE** (any first event)	25 (8.5%)	174 (29.5%)	0.25	0.16– 0.38	**<0.001**
Death (all cause) or MI	11 (3.7%)	38 (6.4%)	0.57	0.29 – 1.12	0.10
Major bleeding	3 (1.0%)	8 (1.4%)	0.75	0.20 – 2.84	0.67
Any bleeding at 12months	9 (3.1%)	28 (4.7%)	0.64	0.30 – 1.36	0.25
Any bleeding at 48h	5 (1.7%)	8 (1.4%)	1.25	0.41 – 3.83	0.69
Hospitalization for heart failure, unstable angina and chest pain	13 (4.4%)	47 (8.0%)	0.54	0.29 – 0.99	**0.04**
Any revascularization	19 (6.4%)	161 (27.3%)	0.47	0.29 – 0.76	**0.002**
Stent thrombosis	2 (0.7%)	1 (0.2%)	0.58	0.12 – 2.80	0.50

Conclusions

- In multivessel STEMI patients, FFR-guided complete revascularization of non-infarct-related lesions in the acute phase of primary PCI significantly reduced the risk of the composite MACCE outcome as compared with a strategy of treatment of the infarct-related artery only

- This reduction was mainly driven by the decreased need for subsequent revascularization

Conclusions

- Approximately half of the lesions in non infarct-related arteries considered significant on coronary angiograms had an FFR value >0.8 and were therefore not physiologically significant

- Deferring treatment of angiographically significant coronary lesions in non-infarct related arteries with an FFR > 0.8 is safe and efficient

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ORIGINAL ARTICLE

Fractional Flow Reserve–Guided Multivessel Angioplasty in Myocardial Infarction

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