Should FFR be used routinely in STEMI patients with multivessel disease ?

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Strategies towards non-IRA lesion

MV-STEMI Patients

Aggressive

MV-PCI acutely

+ *Complete revasc.*
+ *No residual ischemia*
+ *No additional CAG/PCI*
+ *Cost effective*

- *More contrast / radiation*
- *Unstable condition*
- *Thrombogenic milieu*
- *Potential unneeded PCI*

Intermediate

Non-IRA staged

+ *Complete revasc.*
+ *No residual ischemia*
+ *Stable condition*
+ *(Heart team discussion)*

- *Re-CAG*
- *More costs and risk*
- *Potential unneeded PCI*

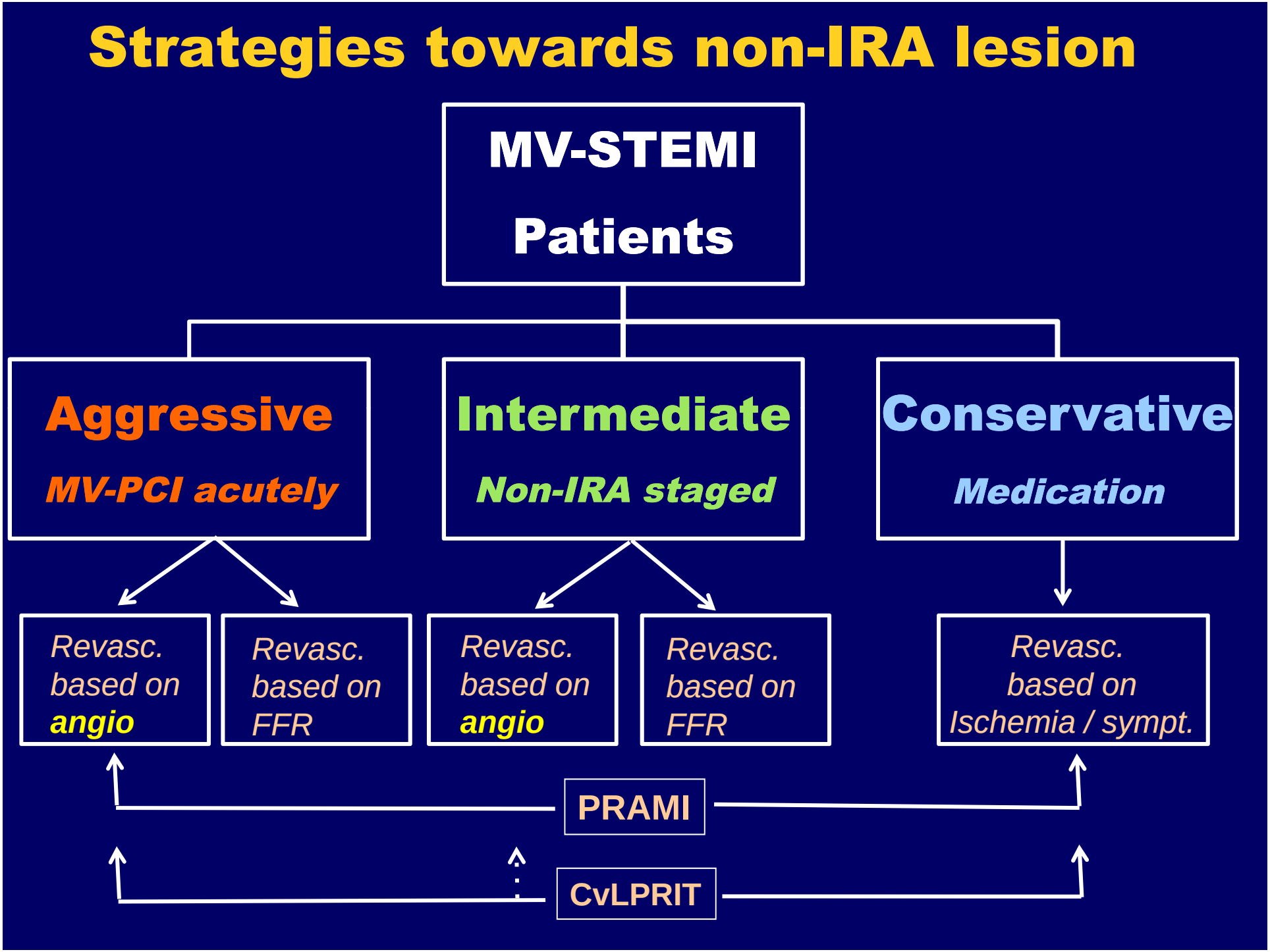
Conservative

Medication

+ *Proper indication revasc.*
+ *Stable condition*
+ *Heart team discussion*

- *Sign. residual ischemia*
- *Non conclusive isch. test*
- *More costs and risk*

Strategies towards non-IRA lesion



Meta-analysis
Acute complete versus Non-complete / Staged

Complete revascularization in the acute phase:

- *41 % Reduction in MACE (death, recurrent MI, Revascularization)*
- *52% Reduction in recurrent MI*
- *49% Reduction in repeat revascularization*
- *Trend towards lower cardiovascular mortality (p=0.09)*

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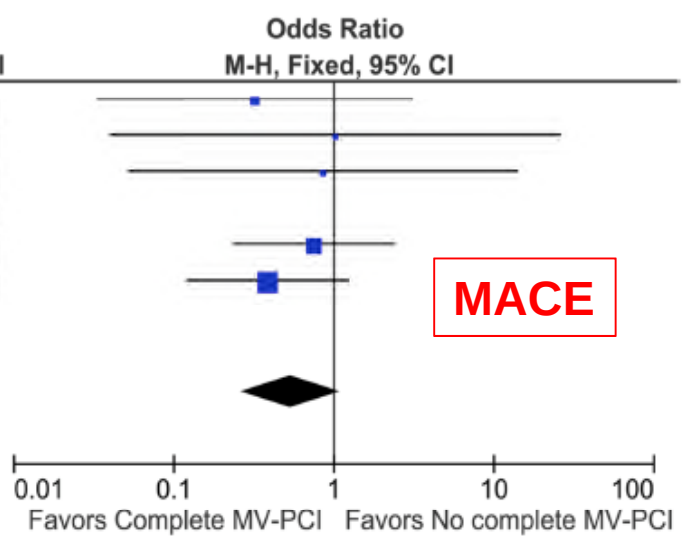
Study or Subgroup	Complete MV-PCI Events	Total	No complete MV-PCI Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
CvLPRIT 2014	1	150	3	146	14.0%	0.32 [0.03, 3.11]
HELP AMI 2004	1	52	0	17	3.4%	1.02 [0.04, 26.19]
Maamoun 2011	1	42	1	36	4.9%	0.85 [0.05, 14.15]
Ochala 2004	0	48	0	44		Not estimable
Politi 2009	4	65	12	149	31.8%	0.75 [0.23, 2.41]
PRAMI 2013	4	234	10	231	45.9%	0.38 [0.12, 1.24]
Tarasov 2014	0	46	0	43		Not estimable
Total (95% CI)		**637**		**666**	**100.0%**	**0.54 [0.26, 1.10]**
Total events	11		26			

Heterogeneity: Chi² = 1.07, df = 4 (P = 0.90); I² = 0%

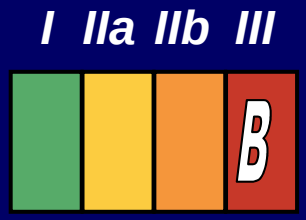
Test for overall effect: Z = 1.69 (P = 0.09)



Kowalski et al. Heart 2015;101:1309-17

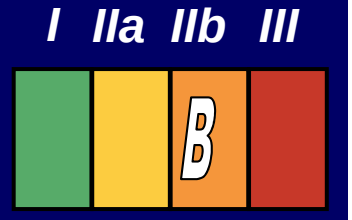
Guidelines

ACC/AHA 2013



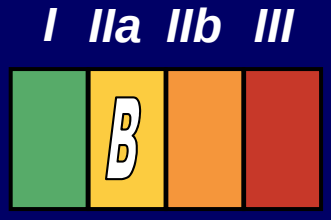
PCI of a non-infarct artery at the time of primary PCI in patients without hemodynamic compromise is not indicated

ACC/AHA/SCAI 2015



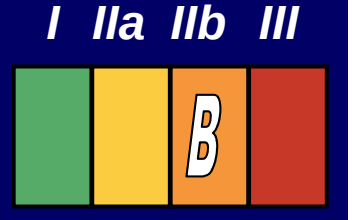
PCI of a noninfarct artery may be considered in selected patients with STEMI and multivessel disease who are hemodynamically stable, either at the time of primary PCI or as a planned staged procedure

ESC 2010



With the exception of cardiogenic shock, PCI (whether primary, rescue, or post-fibrinolysis) should be limited to the culprit stenosis.

ESC/EACTS 2014



Immediate revascularization of significant non-culprit lesions during the same procedure as primary PCI of the culprit vessel may be considered in selected patients

Do all non-IRA lesions with ≥ 50% stenosis by angiography need to be treated acutely ?

Potentially yes:

- Randomized data suggest this strategy
- STEMI patients are known to have more vulnerable plaques
- Less residual ischemic burden

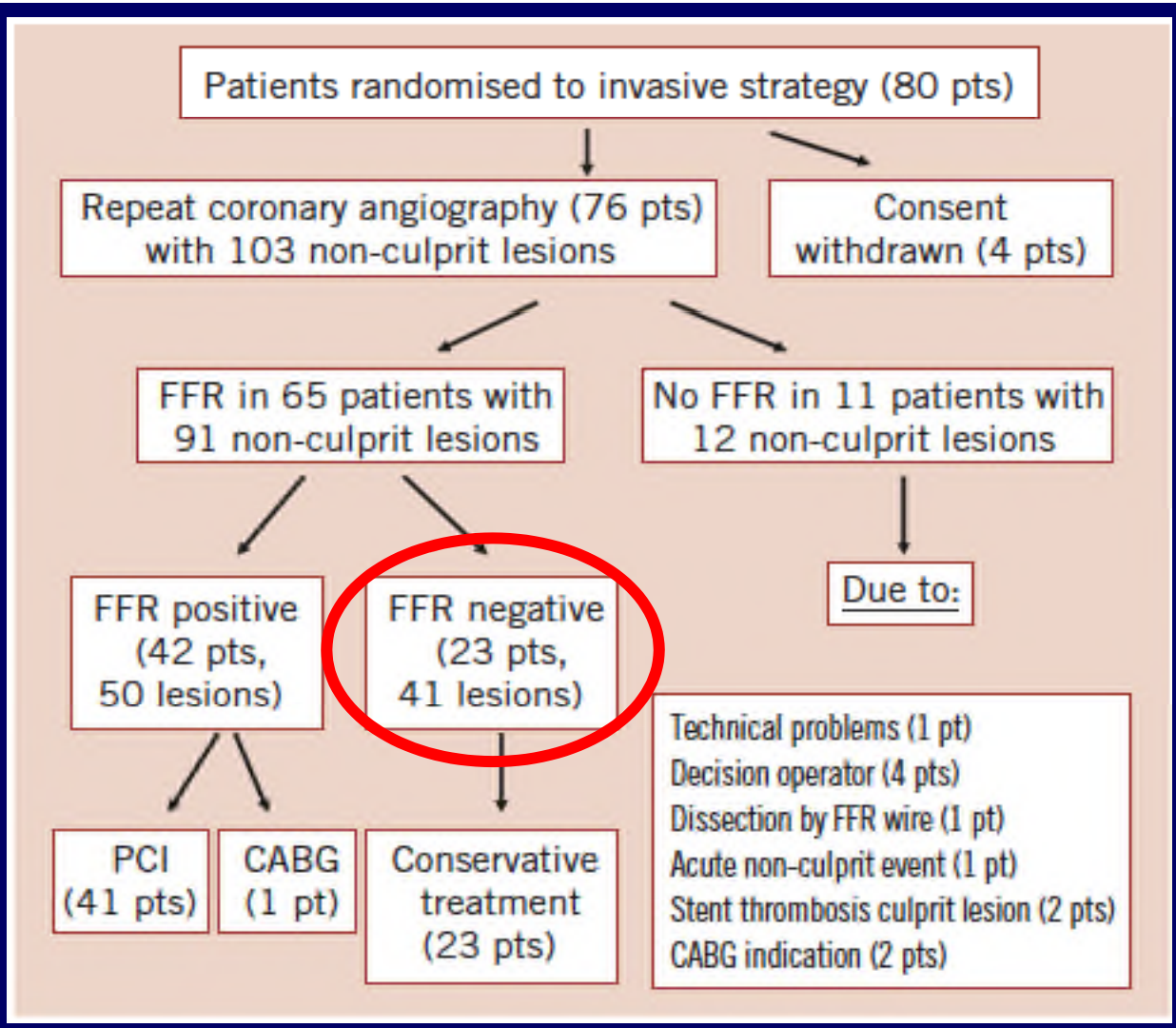
Potentially no:

- Angiography not accurate in determining ischemic or vulnerable lesions
- FFR or OCT / NIRS-IVUS guided revasc. not yet fully investigated
- Limited data about identification true vulnerable plaques
- DEFER & FAME showed that FFR negative lesions are relative benign
- Post STEMI patients receive DAPT and lipid lowering therapy

Non-culprit lesions detected during primary PCI: treat invasively or follow the guidelines?

Jan-Henk E. Dambrink*, MD, PhD; Jan P. Debrauwere, MD; Arnoud W.J. van 't Hof, MD, PhD; Jan-Paul Ottervanger, MD, PhD; A.T. Marcel Gosselink, MD, PhD; Jan C.A. Hoorntje, MD, PhD; Menko-Jan de Boer, MD, PhD; Harry Suryapranata, MD, PhD

Re-CAG + FFR at mean 7.5 days post Prim. PCI



40% of non-IRA lesions are negative with FFR

EuroIntervention 2010;5:968-975

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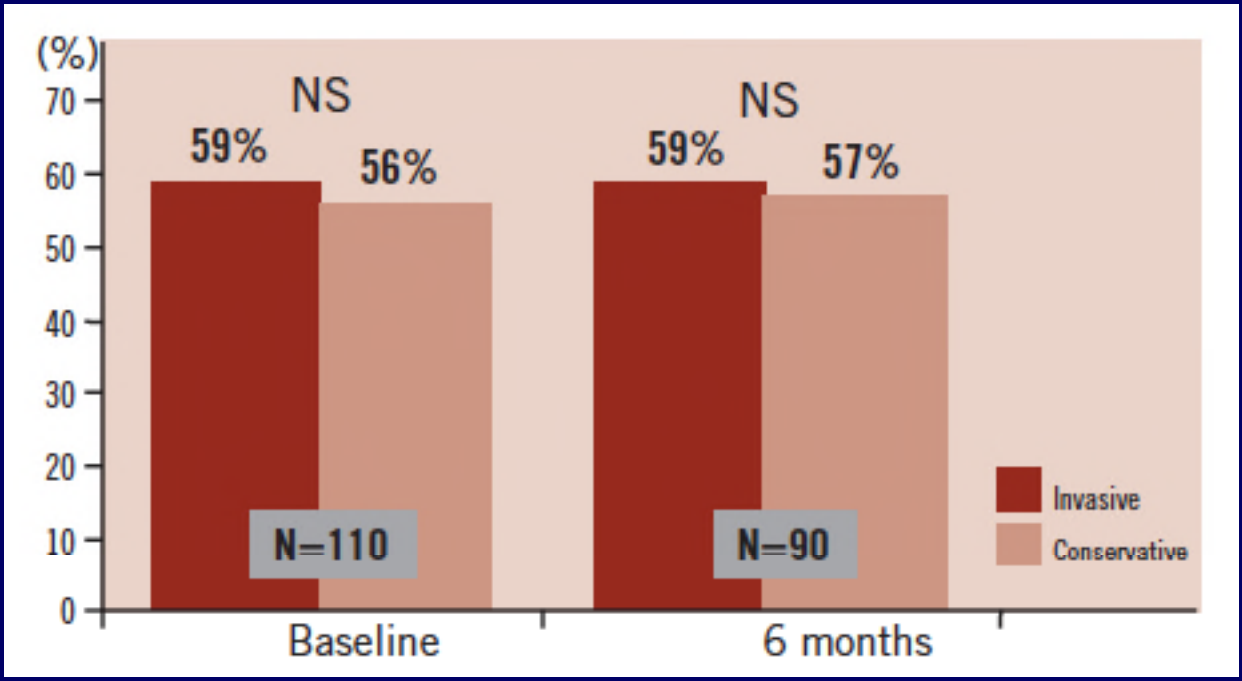
Primary endpoint: Nuclear LVEF @ 6 months



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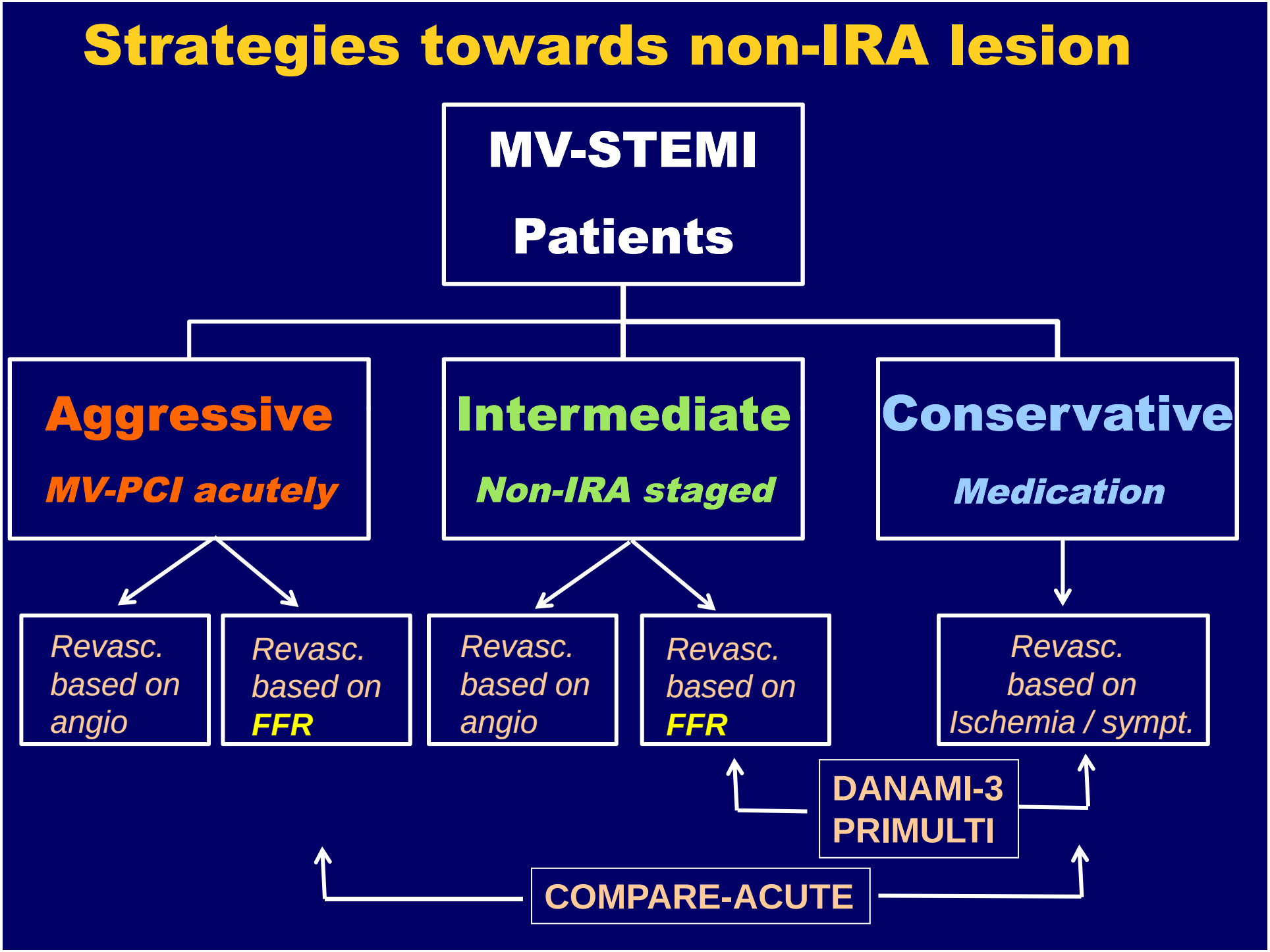
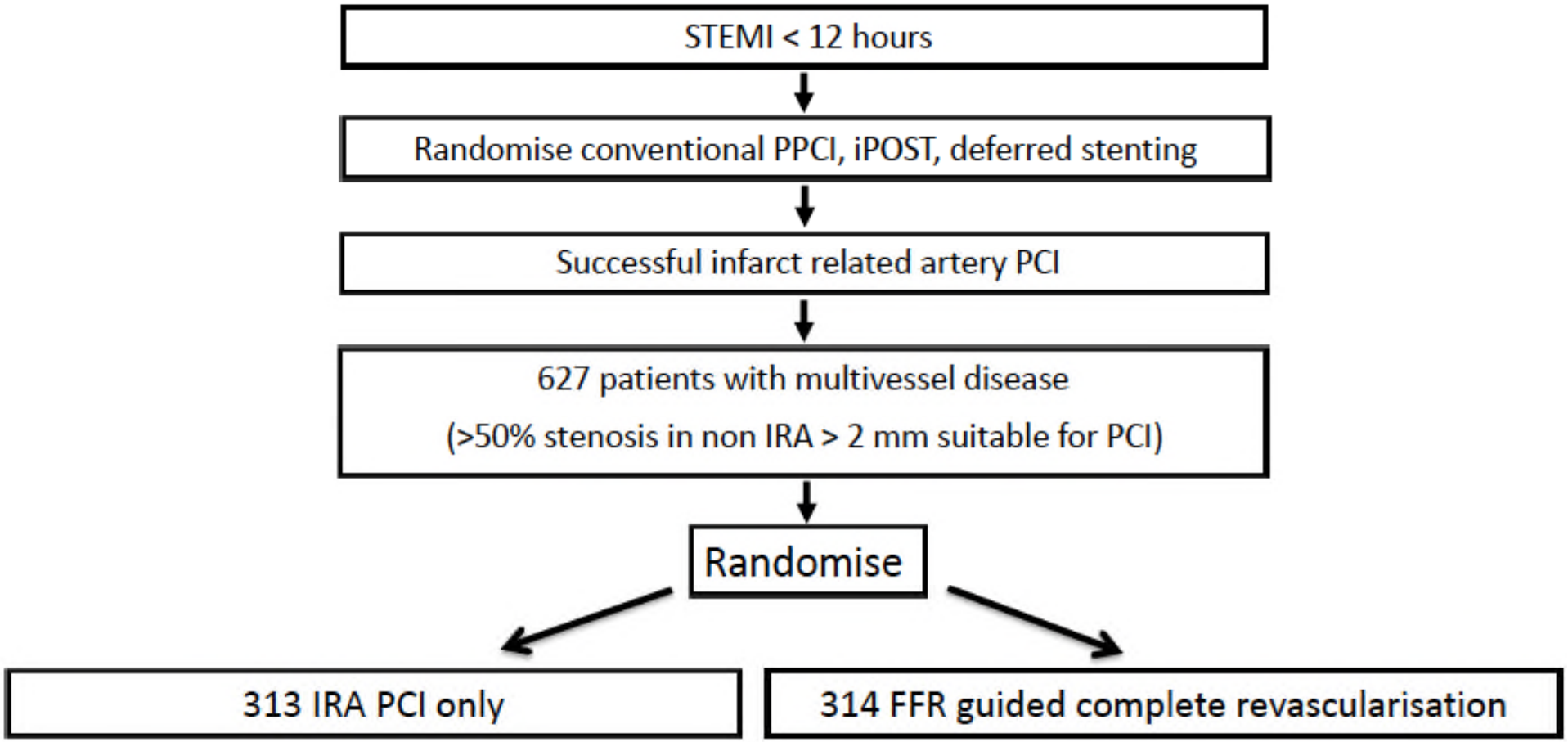
Strategies towards non-IRA lesion



DANAMI3-TRIAL program

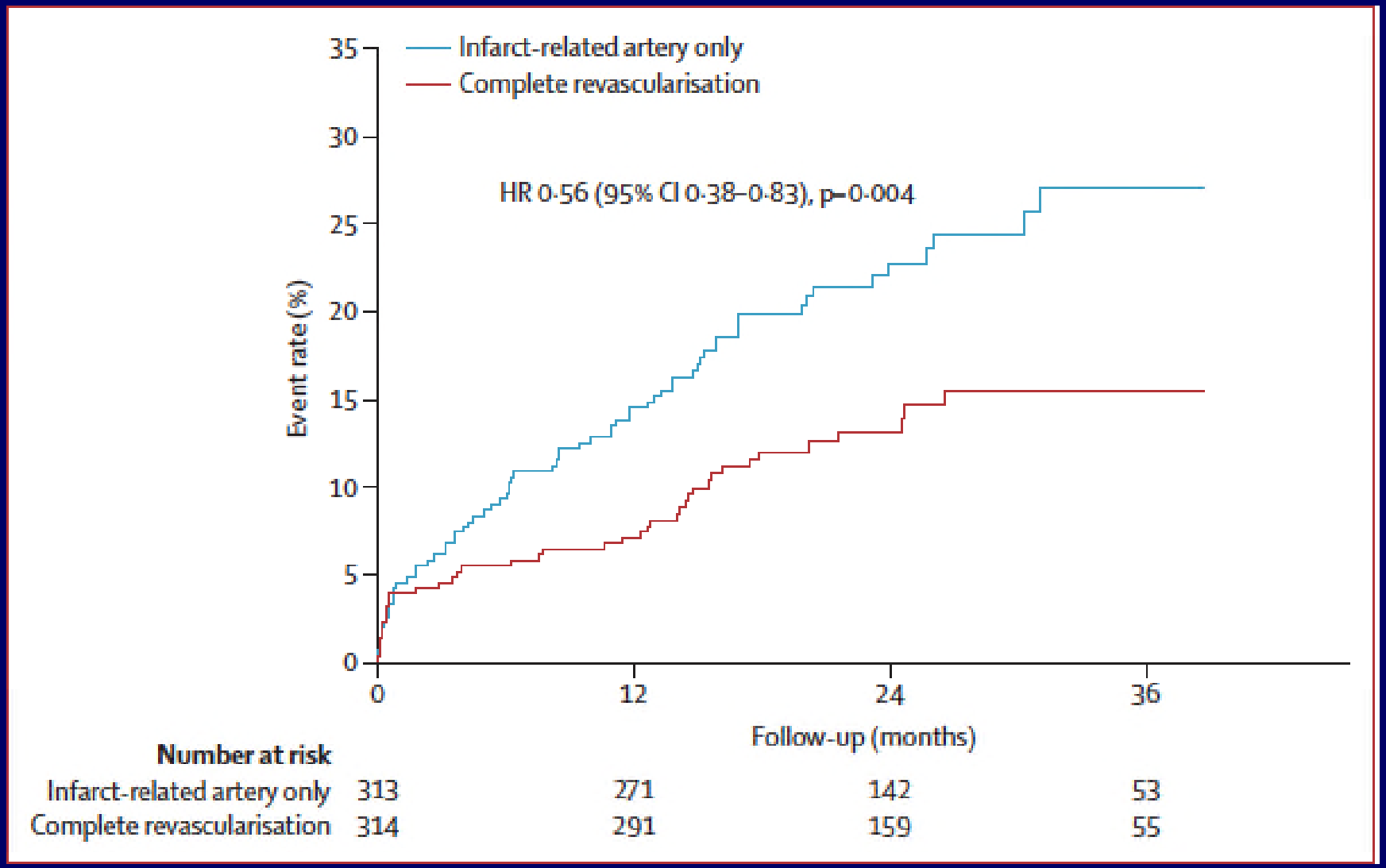


DANAMI3-TRIAL program[1]

[1] Høfsten et al. Am Heart J 2015

DANAMI 3 – PRIMULTI showed benefit for early FFR guided revascularization

Median 27 months FU



***Primary Endpoint (MACE): All** Death, Non fatal MI, ID-Revascularization of non-IRA*

Engstrøm et al. Lancet 2015

DANAMI 3 – PRIMULTI showed benefit for early FFR guided revascularization

Median 27 months FU

	IRA only (n = 313)	Complete revascularisation (n = 314)	HR [95% CI]	p
Primary endpoint	68 (22%)	40 (13%)	0·56 [0·38 – 0·83]	0·004
All-cause death	11 (4%)	15 (5%)	1·4 [0·63 – 3·0]	0·43
Nonfatal MI	16 (5%)	15 (5%)	0·94 [0·47 – 1·9]	0·87
Ischaemia-driven revascularisation*	52 (17%)	17 (5%)	0·31 [0·18 – 0·53]	<0·001
Secondary endpoints				
Cardiac death	9 (3%)	5 (2%)	0·56 [0·19 – 1·7]	0·29
Cardiac death or nonfatal MI	25 (8%)	20 (6%)	0·80 [0·45 – 1·45]	0·47
Urgent PCI	18 (6%)	7 (2%)	0·38 [0·16 – 0·92]	0·03
Non-urgent PCI	27 (9%)	8 (3%)	0·29 [0·13 – 0·63]	0·002

* PCI or CABG

Primary Endpoint mainly driven by repeat revascularization

Engstrøm et al. Lancet 2015

COMPARE-ACUTE trial

COMPARE ACUTE is an prospective, randomized trial carried out at 24 sites across Europe and Asia

Objective is to evaluate the strategy of FFR guided complete revascularization in the acute setting versus the culprit only revascularization strategy

The primary study endpoint is MACCE defined as death, myocardial infarction, any revascularization, or cerebral accident at 12 months.

ClinicalTrials.gov # NCT01399736

MAASSTAD ZIEKENHUIS

Compare Acute

COMPARE-ACUTE trial design

885 STEMI pts + Multi VD
(non IRA ≥ 50%)

Estimated MACCE
8% versus 14.5%
Power 80%

Inclusion criteria:
- *Pts. 18-85 year old*
- *Prim. PCI < 12 hours*
- *Non-IRA lesions ≥ 50%*

by visual assesment and amendable for PCI

After succesfull
Primary PCI of IRA
Randomised

Exclusion criteria:
- *LM ≥ 50% stenosis*
- *Kilip class > 2*
- *Stent thrombosis*
- *CTO*
- *Non-IRA TIMI flow < 3*

R

1:2

FFR of all lesions ≥ 50% stenosis in >2mm non-IRA

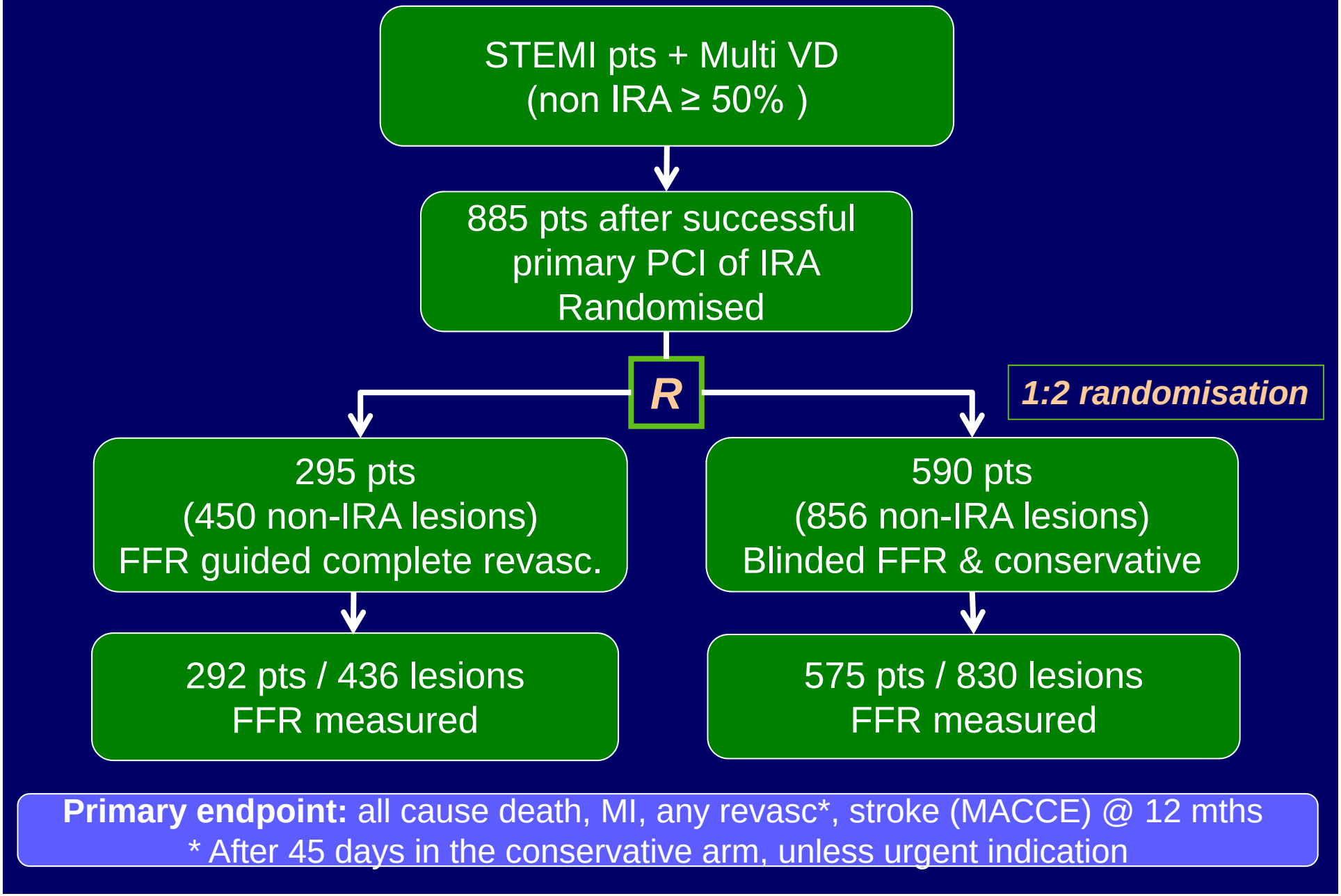
FFR of all lesions ≥ 50% stenosis in >2mm non-IRA

Acute FFR guided complete PCI of non-IRA lesions

Conservative strategy
(Treating cardiologist blinded for FFR value)

Primary endpoint: all cause death, MI, any revasc*, stroke (MACCE) @ 12 mths
* After 45 days in the conservative arm, unless urgent indication

COMPARE-ACUTE trial flow



Primary endpoint: all cause death, MI, any revasc*, stroke (MACCE) @ 12 mths
* After 45 days in the conservative arm, unless urgent indication

FFR of the non-IRA during STEMI

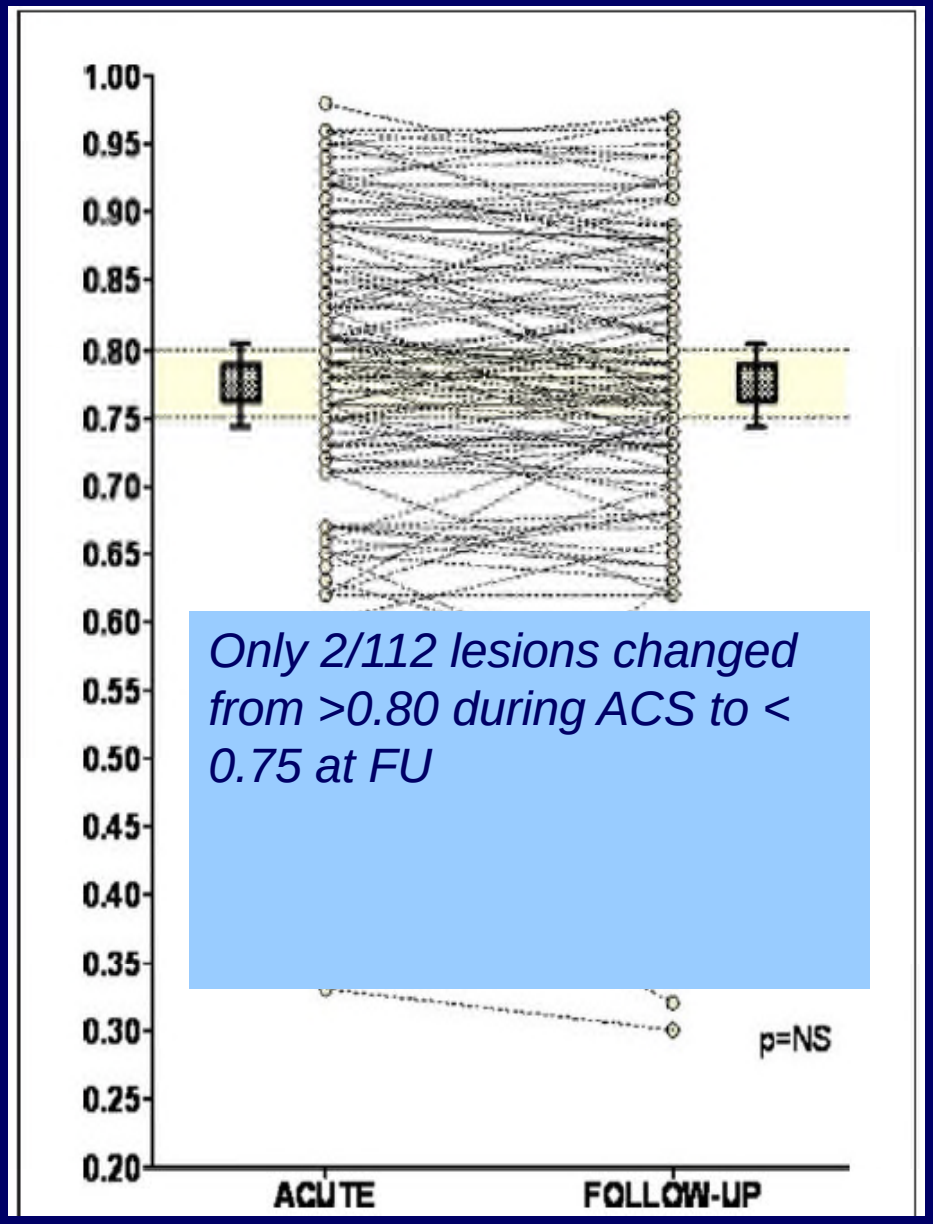
During STEMI, is the FFR of the non infarct related artery reliable ?

Ntalialis et al. JACC CardioVasc Int 2010;12:1274-81

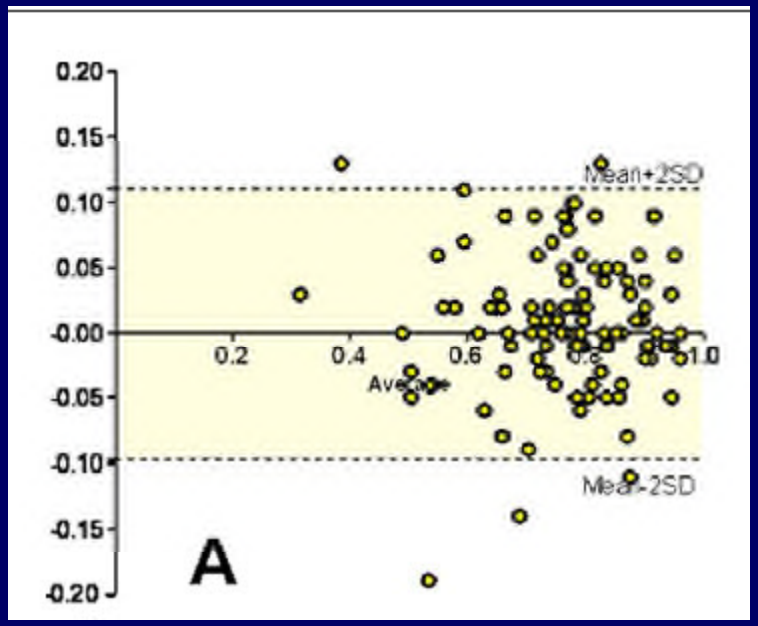
101 AMI patients (75 STEMI, 26 non-STEMI)

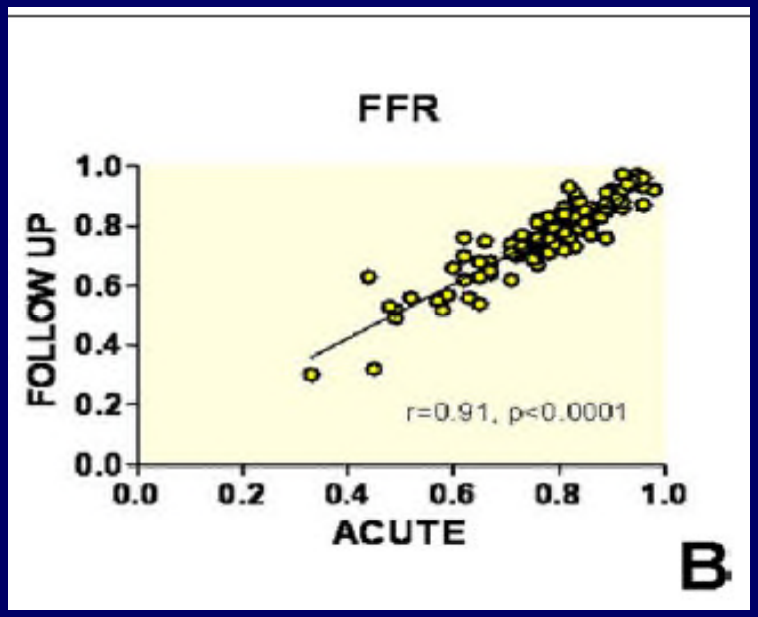
112 non-IRA lesions FFR acutely after P-PCI

Repeat FFR after 35 ± 4 days after PCI



Only 2/112 lesions changed from >0.80 during ACS to < 0.75 at FU





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Why FFR of non-IRA lesions in STEMI patients during pPCI ?

Potential benefits :

- Justified complete or justified incomplete revascularization might improve clinical outcome
- Facilitate decision making in the heart-team
- Expedite post MI care and discharge
- Reduce costs
- Provide patient security

WAVE study design (Rome, Italy)
Started August 2015, Recruiting

60 STEMI pts + Multi VD
(non IRA ≥ 50%)

After succesfull
Primary PCI of IRA

FFR and iFR of non-IRA
Acute stage

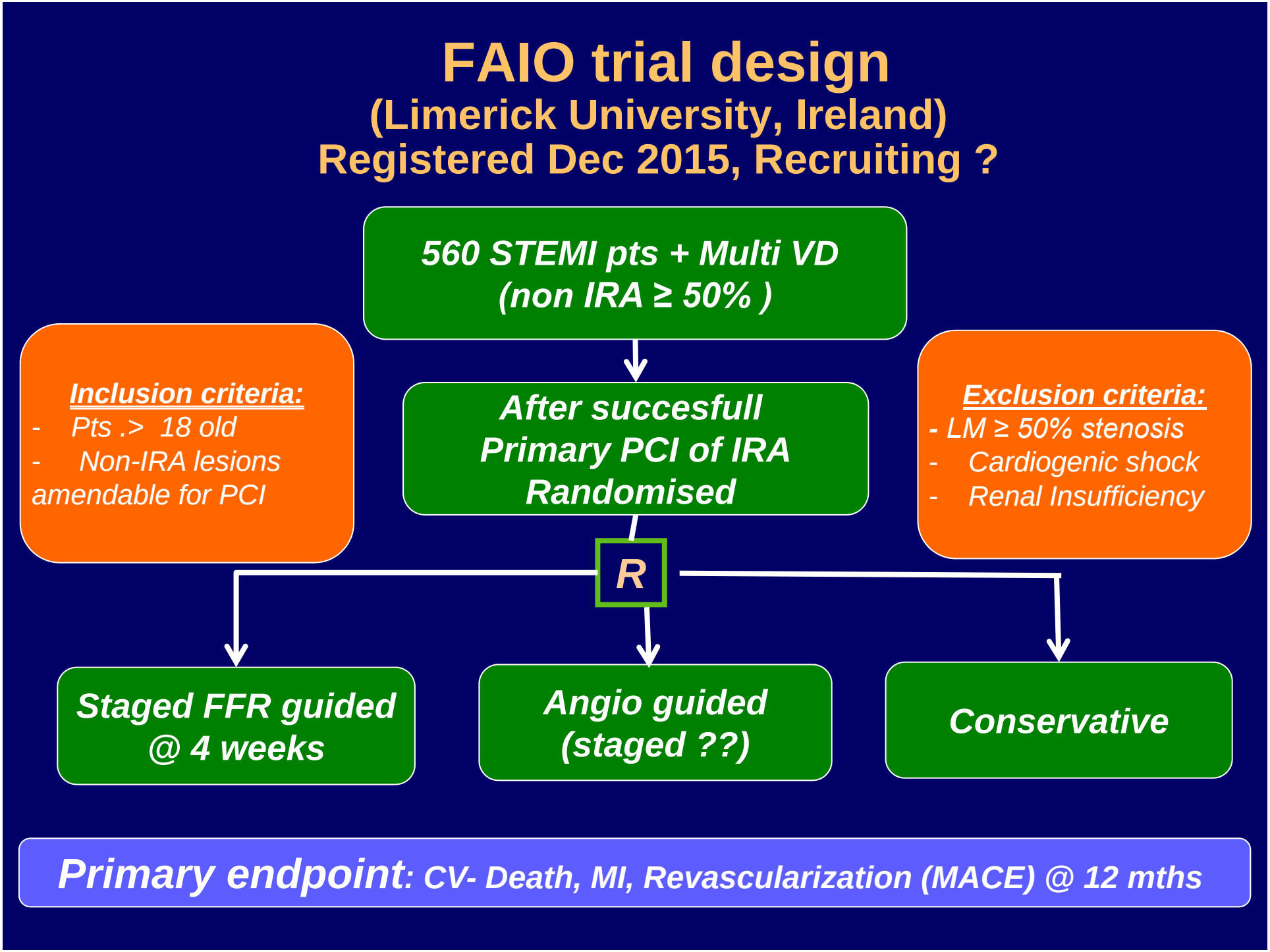
FFR and iFR of non-IRA
Subacute stage 5-7 days

Inclusion criteria:
- *Pts .> 18 old*

Exclusion criteria:
- Sinus bradycardia
- *Heart failure*
- *Previous MI*
- *Poor LVF*

Primary endpoint: assessment reliability FFR and iFR acutely and staged

FAIO trial design
(Limerick University, Ireland)
Registered Dec 2015, Recruiting ?



FRAME-STEMI trial design

(Seoul National University, Korea)

Registered March 2016, Recruiting ?

974 STEMI pts + Multi VD
(non IRA > 50%)

After succesfull
Primary PCI of IRA
Randomised

R

Inclusion criteria:

- *Pts .> 18 old*
- *Non-IRA lesions amendable for PCI*

Exclusion criteria:

- *LM ≥ 50% stenosis*
- *Cardiogenic shock*
- *Renal Insufficiency*
- *CTO*
- *TIMI flow non-IRA < 3*

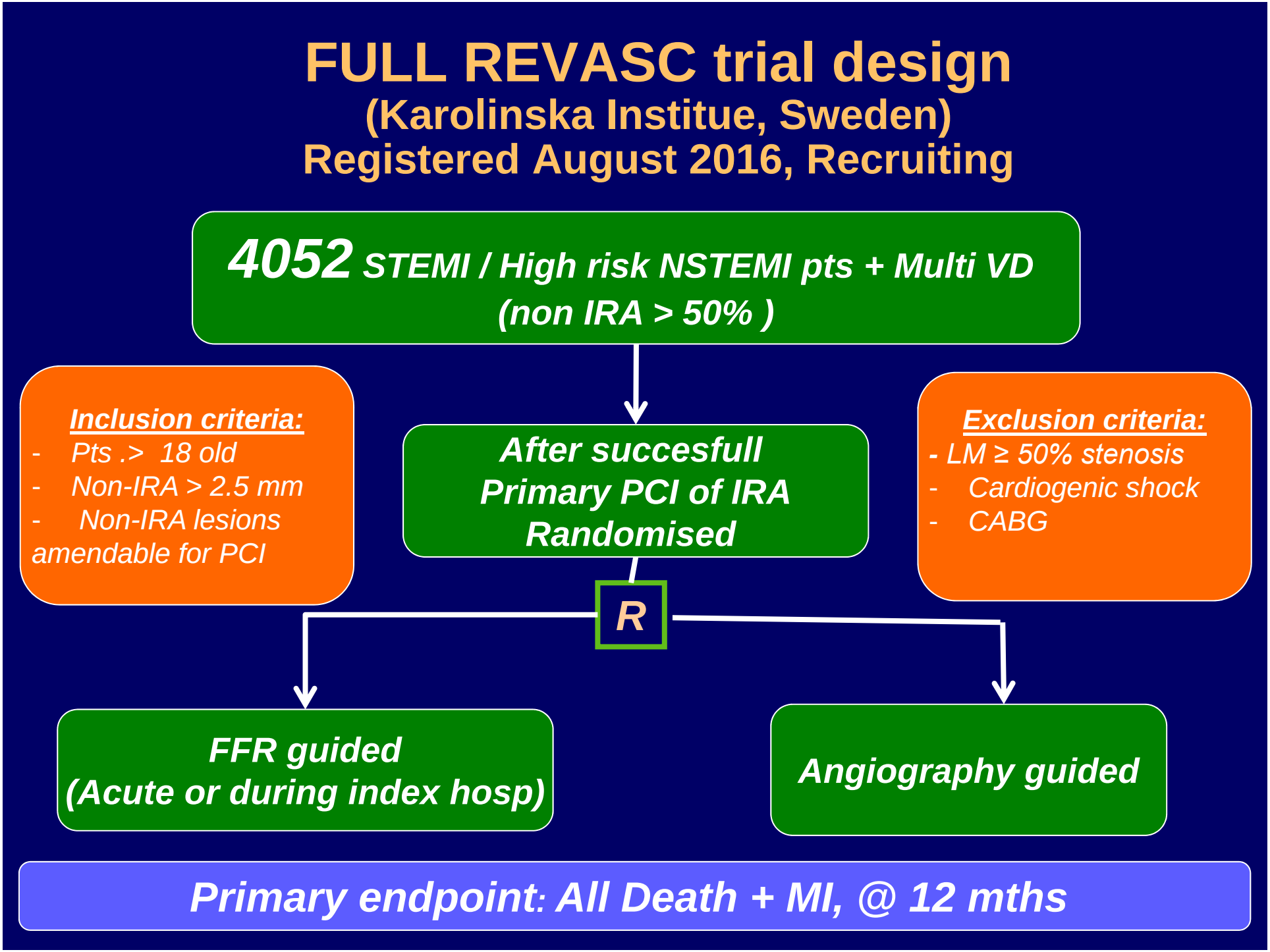
FFR guided
(Acute / staged ?)
Adenosine/ nicorandil

Angiography guided
(Acute / staged ?)

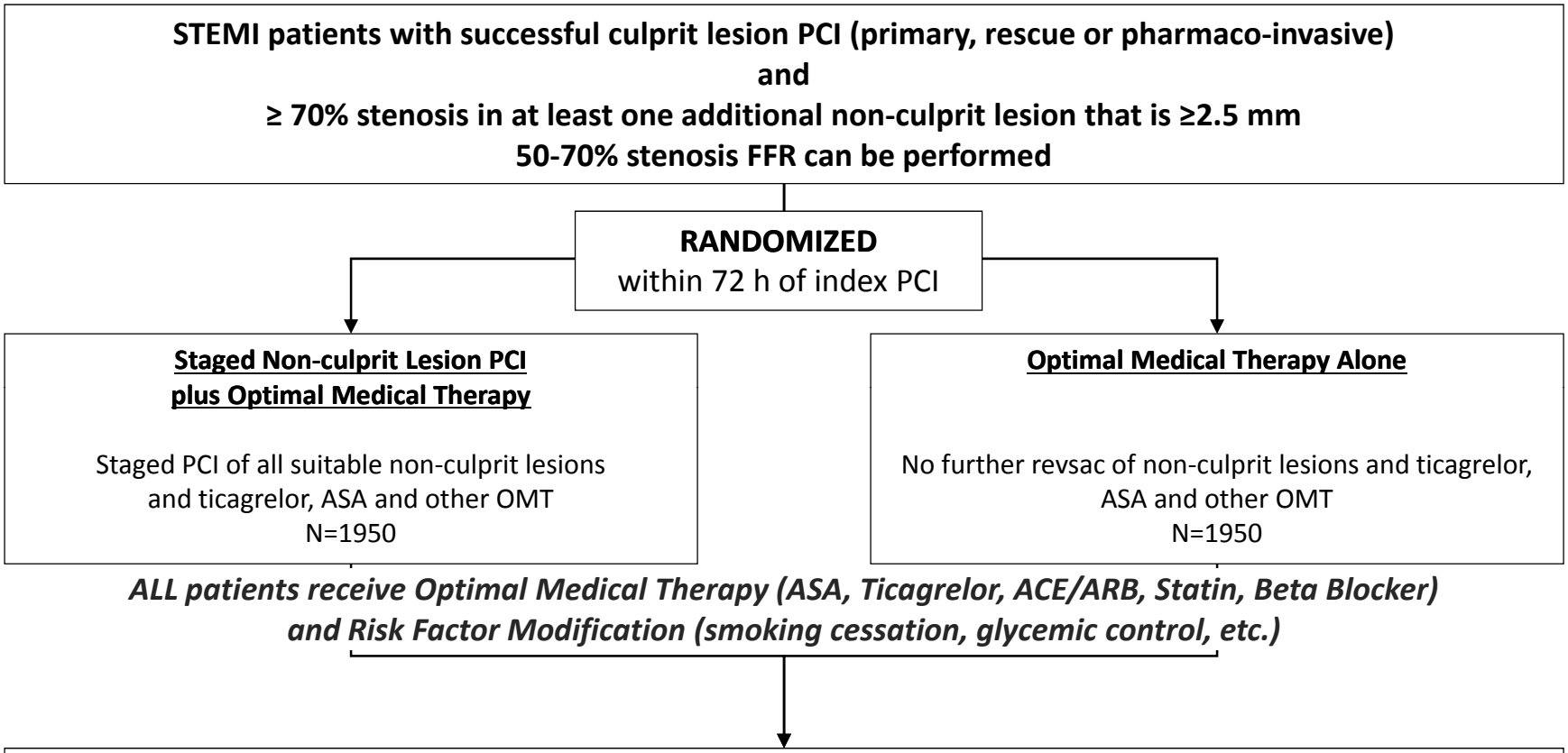
- ***70 % => immed. PCI***
- ***50-70% => isch. test***

Primary endpoint*: Any Death, MI, Revascularization (MACE) @ 12 mths*

FULL REVASC trial design
(Karolinska Institue, Sweden)
Registered August 2016, Recruiting



COMPLETE Study Design



Primary Efficacy Outcome: Cardiovascular Death or new Myocardial Infarction (MI)
Key Secondary Outcome: Cardiovascular Death, new MI, or Ischemia-driven Revascularization

STEMI = ST segment elevation myocardial infarction
PCI = percutaneous coronary intervention
FFR = fractional flow reserve
OMT = optimal medical therapy

Conclusions

Based on the PRAMI and CvLPRIT trials the previous ban on acute non-culprit treatment in STEMI patients has been lifted and is now allowed in ‘selected’ patients (class 2B)

A staged approach with FFR assessment in a later phase seems to be a acceptable alternative, but done early after pPCI

FFR data shows a high portion of negative FFR-measurements in non culprit lesions with visual estimated stenosis of >50% (FAME 37%, Dambrink 40%, DANAMI 31%)

More RCT data on acute and staged FFR guidance expected from COMPARE-ACUTE (ACC 2017), COMPLETE (2018) and FULL-REVASC (2020)