Twelve vs 48 months of dual antiplatelet therapy after drug-eluting stent placement

The OPTIDUAL randomized trial

Gérard HELFT

on behalf of the OPTIDUAL Investigators

Institut de Cardiologie, Hôpital Pitié-Salpétrière, Assistance Publique Hôpitaux de Paris, Université Pierre et Marie Curie Paris, France
IHU, Institute of Cardiometabolism And Nutrition, Hôpital Pitié-Salpétrière Paris, France

Hypothesis

- On a background of aspirin, **continuing clopidogrel for up to 48 months** would be **superior to stopping clopidogrel at 12 months following drug-eluting stent (DES)** implantation in **reducing net adverse clinical events** (composite of death, MI, stroke or major ISTH bleeding)

Helft G et al, Trials 2013;14:56

Inclusion criteria

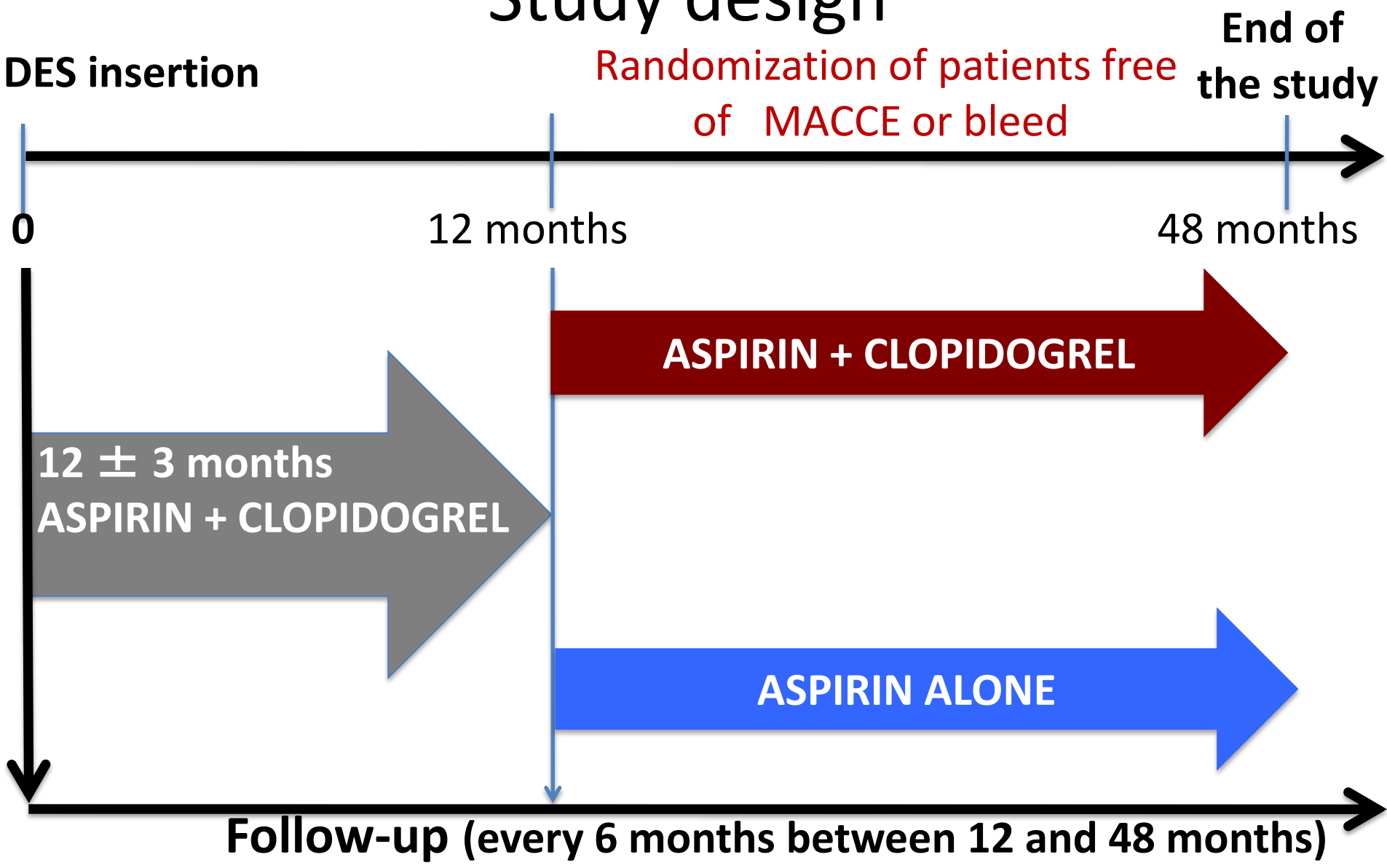
- Patients with stable CAD or ACS
- With ≥1 lesion with a significant stenosis in an artery ≥2.25 mm
- Implanted with ≥1 DES of any type

Exclusion criteria

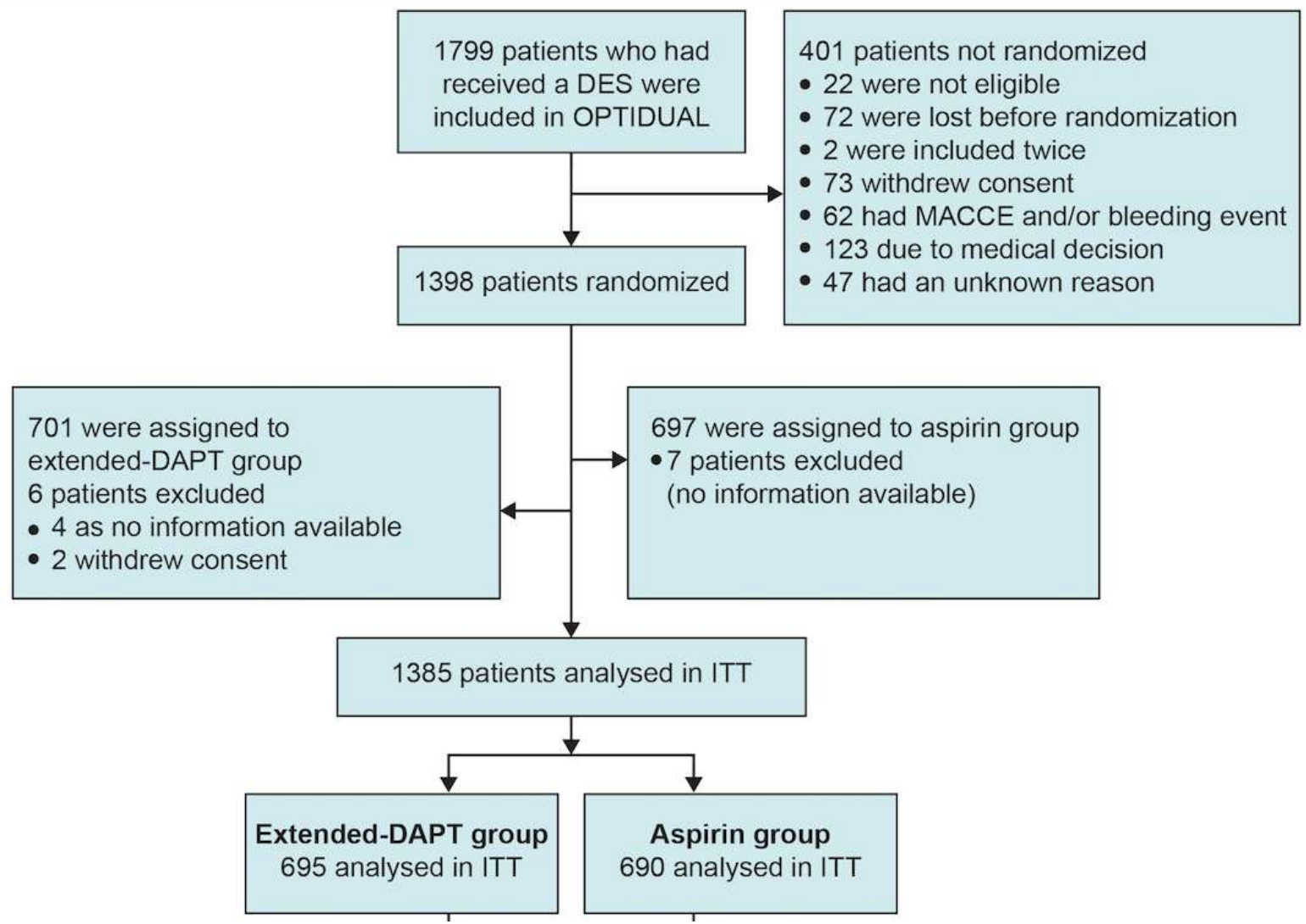
- DES implantation in an unprotected left main coronary artery
- Requirement for oral anticoagulation
- Malignancies or other coexisting conditions associated with a life expectancy of <2 years

Randomized, multicentre, open-label study conducted in 58 sites in France (January 2009–January 2013)
1800 patient

Study design



Patient flow chart (CONSORT)



- Primary endpoint
  - **Net adverse clinical events**: composite of all-cause death, non-fatal MI, stroke, or major bleeding (ISTH classification)
- Secondary endpoints
  - Individual components of the primary outcome
  - Stent thrombosis (defined according to the Academic Research Consortium [ARC])
  - Repeat revascularization of the treated vessel
  - Bleeding (ISTH, GUSTO, TIMI, BARC classifications)

Patient baseline characteristics

	EXTENDED DAPT GROUP n=695	ASPIRIN GROUP n=690	P value
Age (years), mean (SD)	64.1 (10.8)	64.2 (11.5)	0.88
Women	18.3%	20.7%	0.23
Diabetes mellitus	30.6%	32.2%	0.54
Hypertension	57%	60.4%	0.19
Current/recent smoker	61.2%	57.8%	0.21
Previous PCI	25.9%	27.0%	0.66
Previous MI	17.1%	17.7%	0.78
Previous CABG	5.3%	5.1%	0.83
Stroke or TIA	4.2%	3.6%	0.60
Peripheral artery disease	4.9%	6.5%	0.19

Procedural characteristics

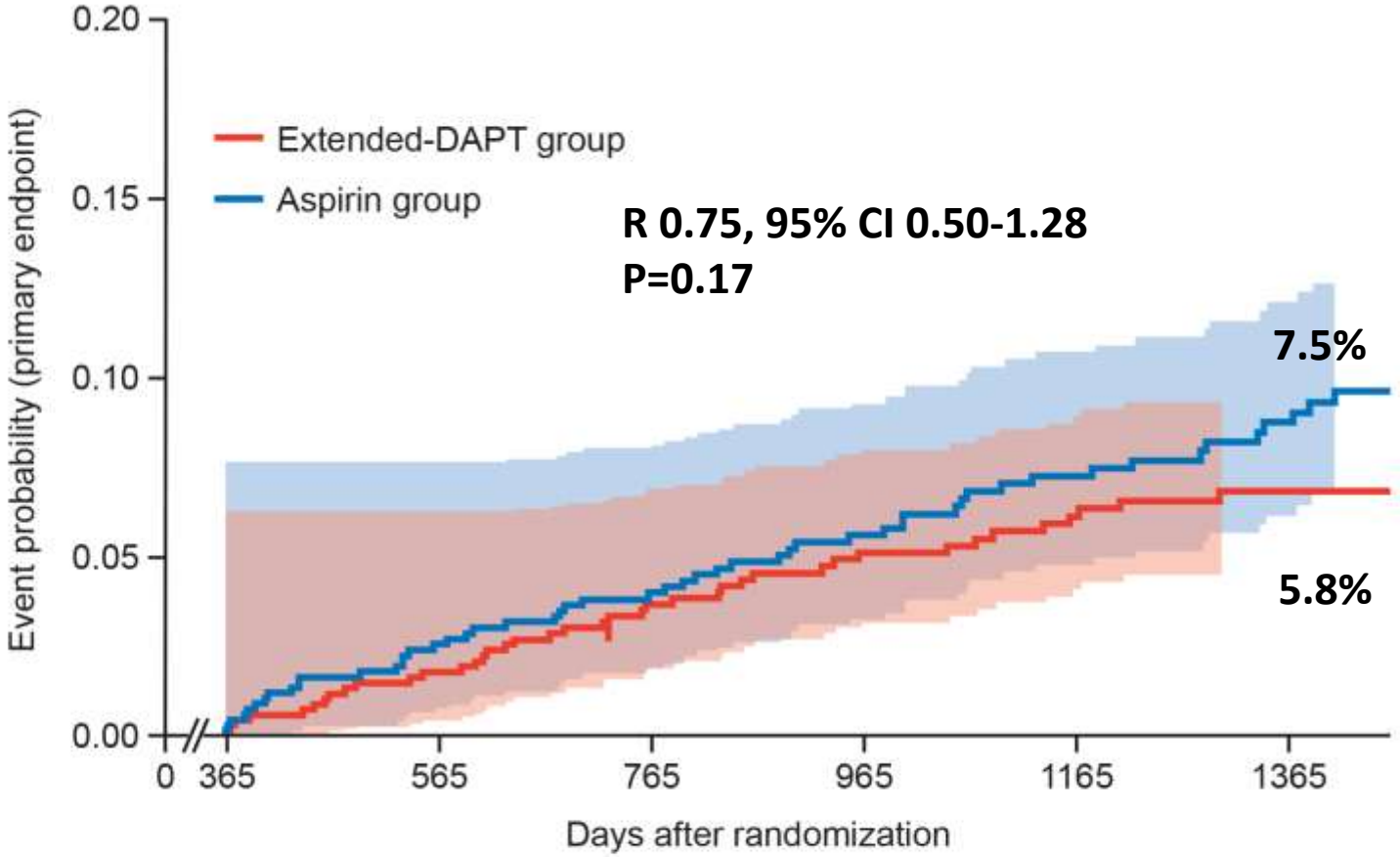
	EXTENDED DAPT GROUP n=695	ASPIRIN GROUP n=690	P value
Indication for PCI			
STEMI	10.7%	11.9%	0.47
Non-STEMI	14.2% (34.4%)	17.0% (38.0%)	0.39
Unstable angina	9.5%	9.1%	0.81
Stable angina	34.5%	30.0%	0.07
Silent ischaemia	19.9% (65.6%)	21.9% (62.0%)	0.35
Other	11.2%	10.1%	0.63
Type of DES			
Sirolimus	19.9% (35.1%)	17.5% (33.5%)	0.17
Paclitaxel	15.2%	16.0%	0.65
Zotarolimus	8.3%	10.8%	0.05
Everolimus	50.2%	49.2%	0.66
Other	6.4%	6. 5%	0.93
Target vessel			
Left main	<1%	>1%	0.69
LAD	58%	64%	0.007
LCX	33%	31%	0.59
RCA	41%	39%	0.58

Treatment at randomization

	EXTENDED DAPT GROUP n=695	ASPIRIN GROUP n=690	P value
Statin	94.4%	93.3%	0.41
ACE inhibitor	75.1%	74.2%	0.71
Proton-pump inhibitor	49.8%	46.8%	0.27
Beta-blocker	78.0%	81.6%	0.09
Calcium-channel inhibitor	30.9%	29.0%	0.43
Aspirin	100%	99.6%	0.12
Daily dose of aspirin at the time of randomization (mg)			0.84
≤100	78.6%	78.2%	
101–300	21.4%	21.8%	

Primary outcome:

Composite of death, MI, stroke, major bleed

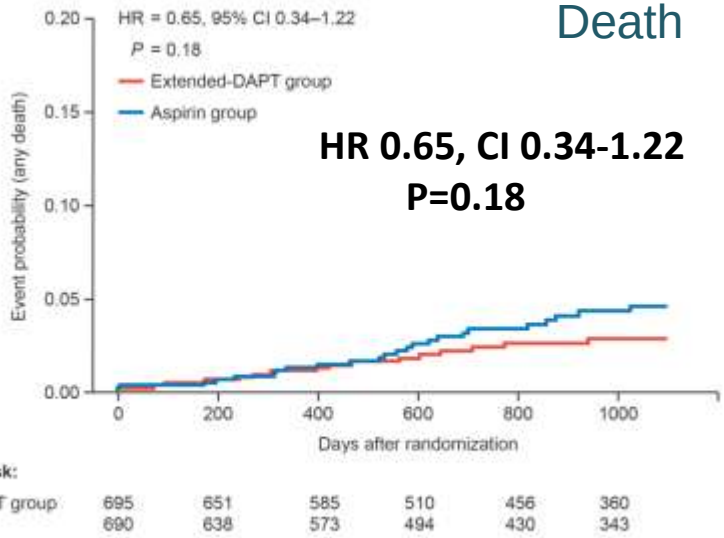


Number at risk:

Extended-DAPT group	695	643	570	493	440	344
Aspirin group	690	626	557	479	415	329

Components of the primary endpoint

Death

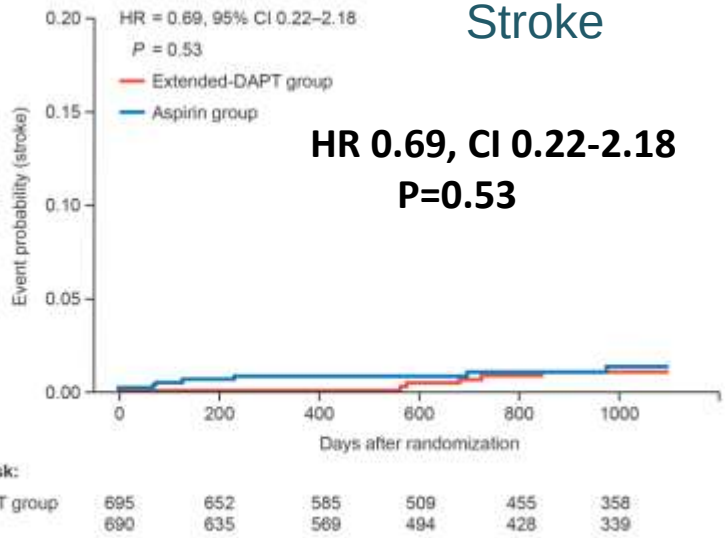


HR 0.65, CI 0.34-1.22
P=0.18

Numbers at risk:

Extended-DAPT group	695	651	585	510	456	360
Aspirin group	690	638	573	494	430	343

Stroke

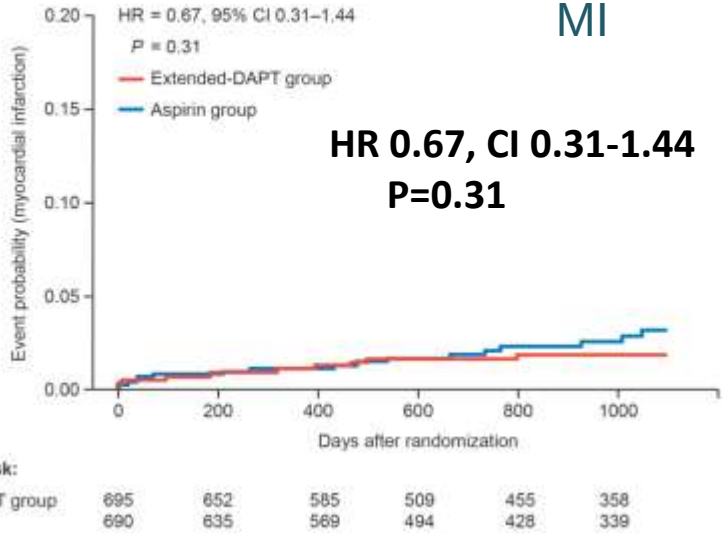


HR 0.69, CI 0.22-2.18
P=0.53

Numbers at risk:

Extended-DAPT group	695	652	585	509	455	358
Aspirin group	690	635	569	494	428	339

MI

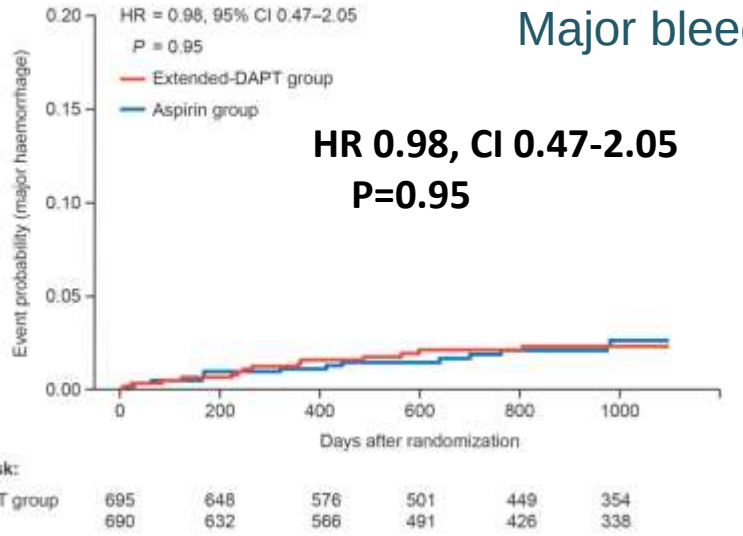


HR 0.67, CI 0.31-1.44
P=0.31

Numbers at risk:

Extended-DAPT group	695	652	585	509	455	358
Aspirin group	690	635	569	494	428	339

Major bleed

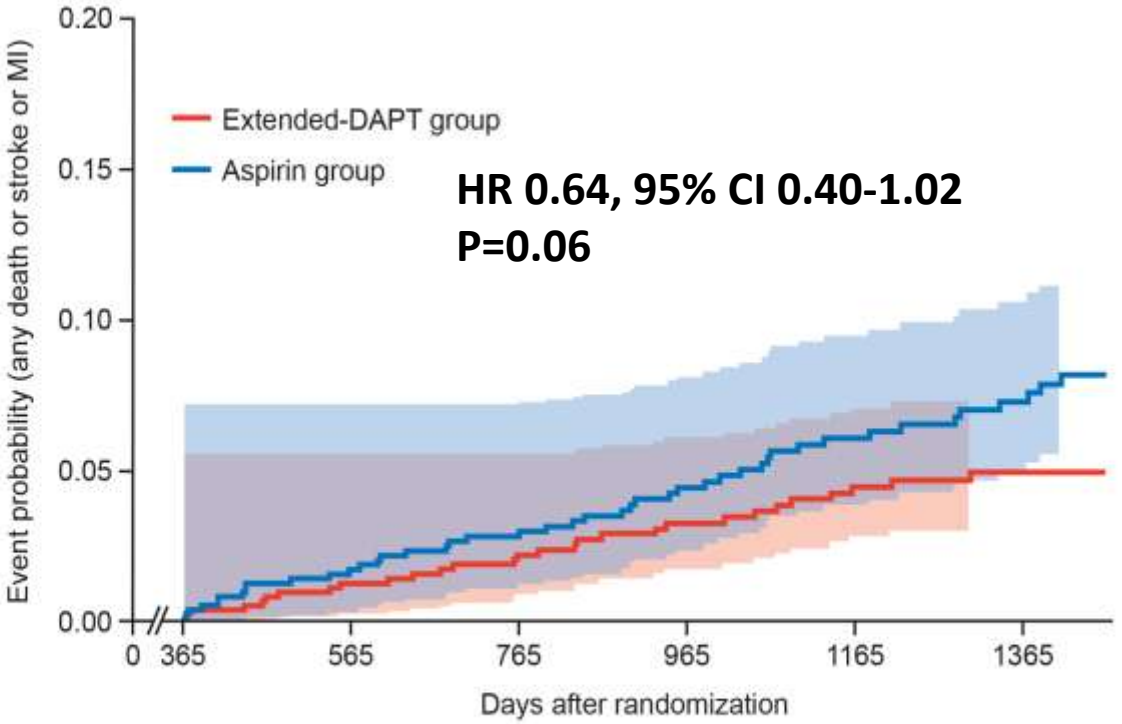


HR 0.98, CI 0.47-2.05
P=0.95

Numbers at risk:

Extended-DAPT group	695	648	576	501	449	354
Aspirin group	690	632	566	491	426	338

Post-hoc analysis of ischaemic outcomes: death, stroke, or MI



Number at risk:

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Conclusions (1)

Extending DAPT duration for up to 48 months **did not achieve statistical superiority** compared with stopping clopidogrel at 12 months with regards to net adverse clinical outcomes, in patients free of MACCE and major bleed 12 months after stent implantation

Conclusions (2)

- Borderline but non-statistically significant reduction in post-hoc analysis of ischaemic outcomes with extended DAPT
- No apparent increase in bleeding and all-cause mortality with extended DAPT

Universitätsklinikum Hamburg-Eppendorf

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BACC (Biomarkers in Acute Cardiovascularcare)

Accurate and Rapid Diagnosis of Myocardial Infarction Using a High-Sensitivity Troponin I 1-Hour Algorithm

Johannes Tobias Neumann[1], Nils Arne Sörensen[1], Tjark Schwemer[1], Francisco Ojeda[1], Rafael Bourry[1], Vanessa Sciacca[1], Sarina Schäfer[1,2], Christoph Waldeyer[1], Christoph Sinning[1], Thomas Renné[3], Martin Than[5], Will Parsonage[4], Karin Wildi[6], Nataliya Makarova[1,2], Renate B. Schnabel[1,2], Ulf Landmesser[7], Christian Mueller[6], Louise Cullen[4], Jaimi Greenslade[4], Tanja Zeller[1,2], Stefan Blankenberg[1,2], Mahir Karakas[1,2], **Dirk Westermann[1,2]**

[1] **Department of General and Interventional Cardiology, University Heart Center Hamburg Eppendorf, Hamburg, Germany**
[2] German Center for Cardiovascular Research (DZHK), Partner Site Hamburg/Kiel/Lübeck, Hamburg, Germany
[3] Institute of Clinical Chemistry and Laboratory Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
[4] Royal Brisbane and Women's Hospital, Department of Emergency Medicine, Brisbane 4006, Australia
[5] Christchurch Hospital, Christchurch, New Zealand
[6] Department of Cardiology and Cardiovascular Research Institute Basel (CRIB), University Hospital Basel, Switzerland
[7] Department of Cardiology, Charite Universitätsmedizin Berlin, Campus Benjamin Franklin, Berlin, Germany

Background

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- There is clinical need to rapidly and safely **rule-in** or **rule-out acute myocardial infarction (AMI)** in patients with acute chest pain in order to

  1. initiate fast evidence based treatment for patients with AMI

  2. limit overuse of scarce medical resources in the emergency room (ER) discharging patients without acute cardiac conditions.

- Guidelines recommend[1,2] measuring high sensitivity assayed troponins directly **after admission and after 3 hours** detecting elevated levels based on the **99th percentile** of the specific assays together with an increase/decrease. (27 ng/l)

- Recent studies (ADAPT (2-hour)[3] and APACE (1- hour)[4] cohort) challenge current guidelines with intervals shorter than 3 hours.

1 Hamm et al. EHJ 2011 and 2 Thygesen et al. EHJ 2012; 3 Than et al. JACC 2012; 4 Reichlin et al. CMAJ 2015

Aim of the study

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To investigate the application of
high sensitivity assayed troponin I (TnI) for

a) a rapid 1-hour rule-out and rule-in compared to a 3-hours approach

b) a lower and more sensitive cut-off value compared to the 99th percentile

in the Biomarkers in Acute Cardiovascular Care (BACC) cohort
investigating 1,045 patients with acute chest pain.

Study design

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BACC (n = 1,045) patients with acute chest pain suggestive of AMI:

Clinical routine troponin assay and clinical treatment based on ESC guidelines[1]:

+ clinical judgement, imaging and ECG to establish final diagnosis during the complete hospital stay

(NSTEMI vs. no AMI)

(as recommended by ESC guidelines[1])

hsTnT: troponin T assay **(**Elecsys® troponin T high sensitive, Roche Diagnostics)

1 Hamm et al. EHJ 2011

Study design

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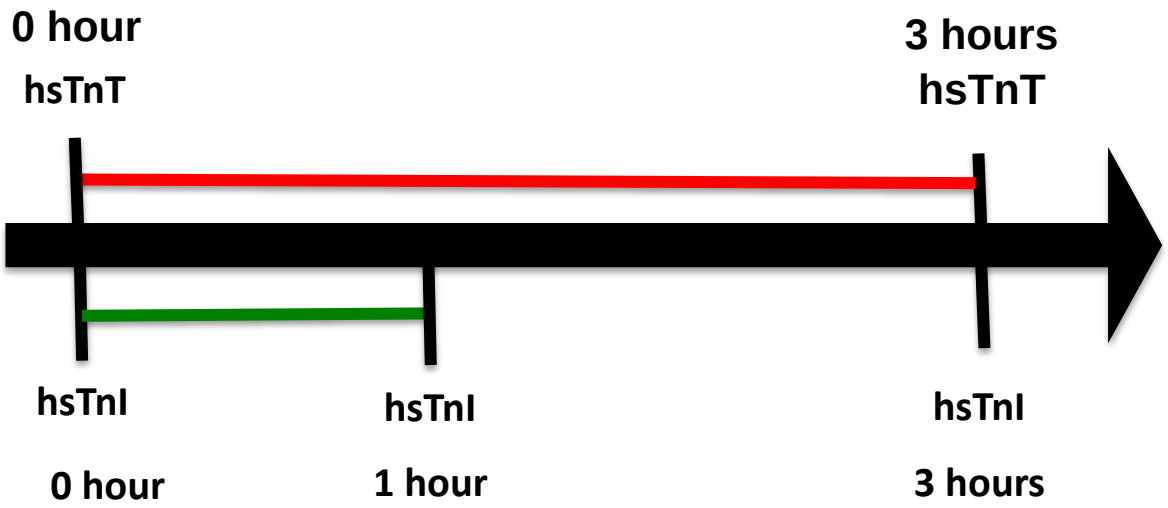

+ clinical judgement, imaging and ECG to establish final diagnosis during the complete hospital stay

(NSTEMI vs. no AMI)

(as recommended by ESC guidelines[1])

+ without adding additional information

hsTnT: troponin T assay **(**Elecsys® troponin T high sensitive, Roche Diagnostics)

hsTnI: troponin I assay (STAT high sensitive Troponin I, ARCHITECT i2000SR, Abbott Diagnostics, USA)

1 Hamm et al. EHJ 2011

Study design

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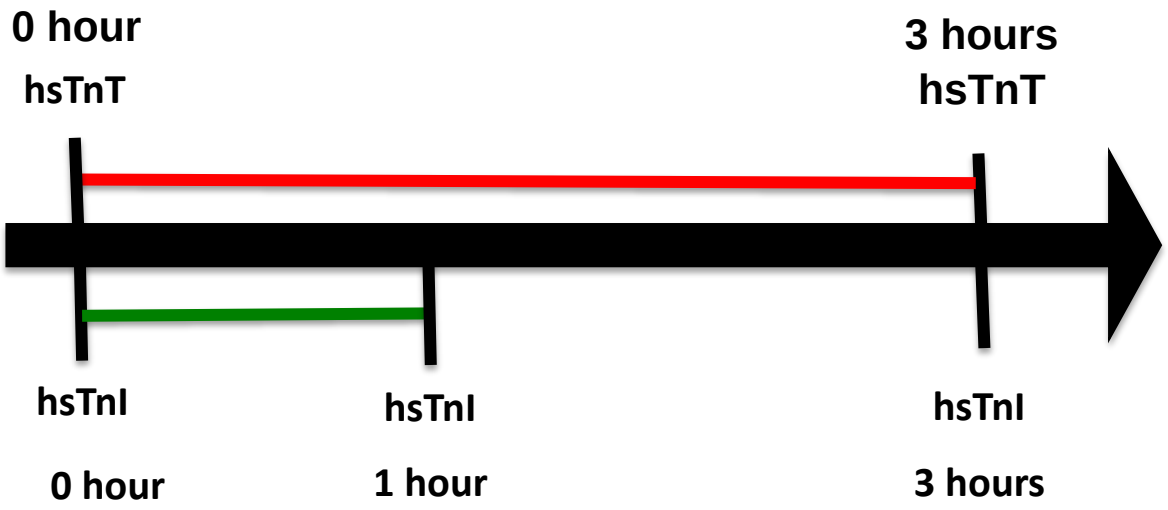

+ clinical judgement, imaging and ECG to establish final diagnosis during the complete hospital stay

(NSTEMI vs. no AMI)

(as recommended by ESC guidelines[1])

+ without adding additional information

Calculate best performing cut-off and apply it → Validate results in other cohorts → Applicate cut-off in general population

1 Hamm et al. EHJ 2011

Baseline data

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	All (N=1,045)	NSTEMI (N=184)	Non-AMI (N=793)	p-value
Demographics				
Age (years)	65.0 (52.0, 75.0)	70.0 (60.4, 77.0)	64.0 (50.7, 74.0)	< 0.001
Male (%)	678 (64.9)	124 (67.4)	505 (63.7)	n.s.
BMI (kg/m²)	26.0 (23.5, 29.4)	26.2 (23.7, 29.7)	26.0 (23.5, 29.4)	n.s.
Risk Factors				
Hypertension (%)	731 (70.0)	147 (79.9)	541 (68.2)	0.0017
Hyperlipoproteinemia (%)	459 (43.9)	103 (56.0)	327 (41.2)	< 0.001
Diabetes (%)	150 (14.5)	39 (21.3)	102 (12.9)	0.0051
Former smoker (%)	334 (32.0)	59 (32.1)	259 (32.7)	n.s.
Current smoker (%)	241 (23.1)	41 (22.3)	169 (21.3)	n.s.
History of CAD/Bypass/PCI (%)	353 (33.8)	80 (43.5)	255 (32.2)	0.0044
History of AMI (%)	165 (15.8)	41 (22.4)	114 (14.4)	0.0097

STEMI (57) and SAP (11) patients were excluded from the non-AMI group

Best performing cut-off

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	NSTEMI 1	
Cut-off (ng/L)	NPV (95% CI)	False Negative
3	100.0 (97.1-100.0)	0
4	99.6 (98.0-100.0)	1
5	99.7 (98.3-100.0)	1
5,2 (10% coefficient of variation)	99.7 (98.4-100.0)	1
6	99.7 (98.6-100.0)	1
7	99.6 (98.4-99.9)	2
8	99.4 (98.3-99.9)	3
9	99.4 (98.4-99.9)	3
10	99.3 (98.2-99.8)	4
15	98.9 (97.8-99.6)	7
20	98.8 (97.7-99.5)	8
27 (99th percentile)	98.4 (97.2-99.2)	11

Rule-out AMI 1h vs. 3h

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Suggested 1-hour algorithm
<u>NSTEMI rule-out:</u>
hsTnI ≤ **6 ng/L** at 0h and 1h

resulted in 402 out of 1,045 patients being discharged

Cut-off	Time after admission	NPV NSTEMI 1 (95% CI)	Sensitivity NSTEMI 1 (95% CI)	NPV NSTEMI (95% CI)	Sensitivity NSTEMI (95% CI)
6ng/L	1-hour	99.7 (98.6-100.0)	99.1 (94.9-100.0)	99.0 (97.5-99.7)	97.6 (94.1-99.4)
	3-hour	100.0 (98.5-100.0)	100.0 (94.9-100.0)	99.5 (98.1-99.9)	98.8 (95.8-99.9)
		p = n.s. vs. 1h		**p = n.s. vs. 1h**	

NPV: negative predictive value; NSTEMI 1: non STEMI type 1 in view of Thygesen K et al. EHJ 2012

Best performing Rule-In Algorithm

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Suggested 1-hour algorithm
<u>NSTEMI rule-in:</u>

hsTnI after 1h > **6 ng/L** together with a delta of **12 ng/L** to 0h

Criteria to diagnose patients as NSTEMI	PPV NSTEMI 1 (95% CI)	Specificity NSTEMI 1 (95% CI)	PPV NSTEMI (95% CI)	Specificity NSTEMI (95% CI)
1-hour rule-in	82.8 (73.2-90.0)	98.0 (96.7-98.9)	87.1 (79.6-92.6)	98.0 (96.7-98.9)
3-hour rule-in	78.6 (69.8-85.8)	96.8 (95.2-97.9)	84.6 (78.0-89.9)	96.8 (95.2-97.9)
	p = n.s. vs. 1h		**p = n.s. vs. 1h**	

PPV: positive predictive value; NSTEMI 1: non STEMI type 1 in view of Thygesen K et al. EHJ 2012

Validation in 2 independent cohorts

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	ADAPT (2-hour)		APACE (1-hour)	
	Non-AMI	NSTEMI	Non-AMI	NSTEMI
Number of patients	1,499	249	1,832	429
Age, years, Median	59 (49-70)	71 (60-79)	59 (47-73)	72 (59-80)
Male gender (%)	868 (57.9)	163 (65.5)	1,226 (66.9)	316 (73.7)

Rule used to diagnose *all* NSTEMI	NPV for rule-out (95% CI)	PPV for rule-in (95% CI)
Troponin I	**APACE[1]**	
Rule-out algorithm (≤ 6 ng/L and after 1h ≤ 6 ng/L)	99.2 (98.4-99.6)	
Rule-in algorithm (1h > 6 ng/L and ≥ 12 ng/L)		80.4 (75.1-84.9)
Troponin I	**ADAPT[2]**	
Rule-out algorithm (≤ 6 ng/L and after 2h ≤ 6 ng/L)	99.7 (99.2-99.9)	
Rule-in algorithm (1h > 6 ng/L and ≥ 12 ng/L)		81.5 (75.8-86.3)

1 Reichlin et al. CMAJ 2015, 2 Than et al. JACC 2012

Follow-up mortality

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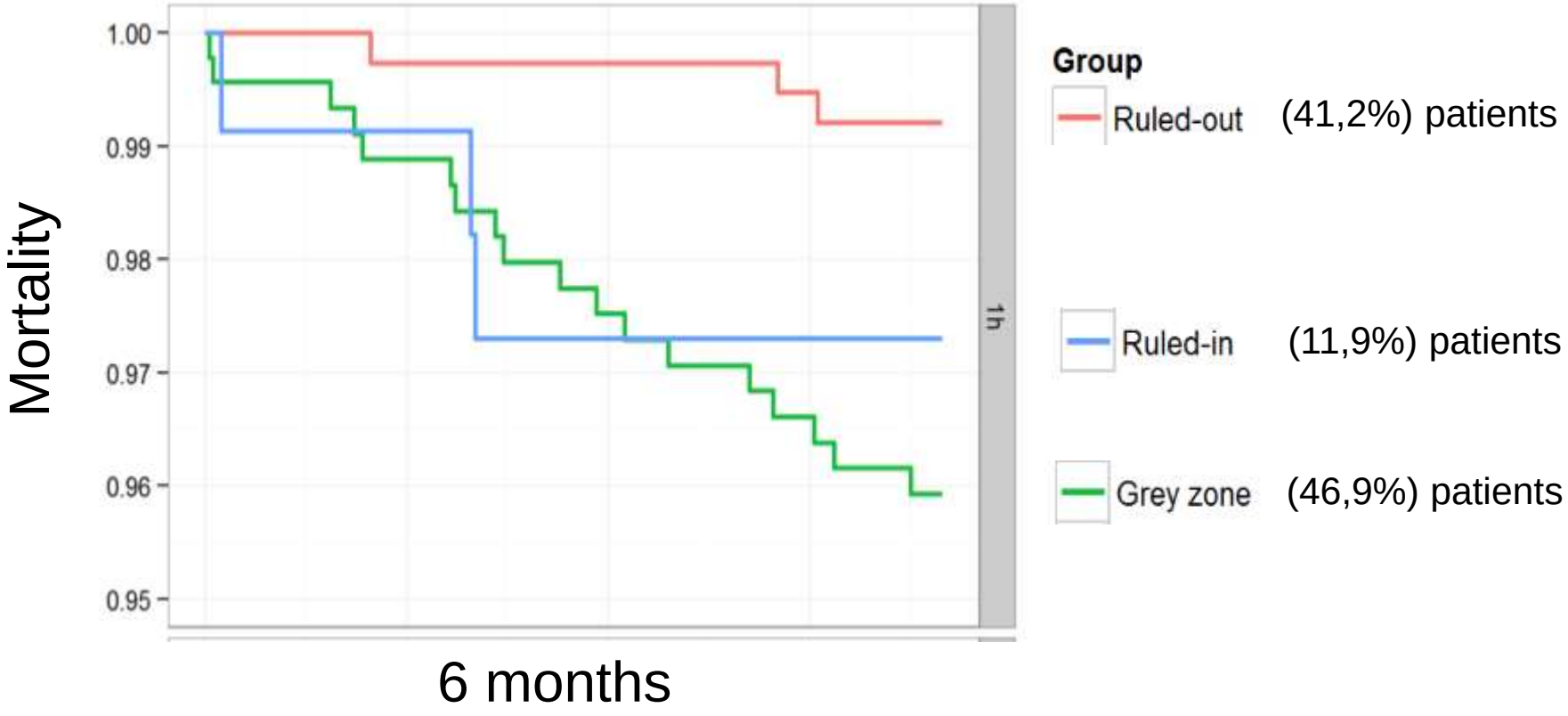
Suggested 1-hour algorithm

NSTEMI rule-out: hsTnI ≤ **6 ng/L** at 0h and 1h

NSTEMI rule-in: hsTnI after 1h > **6 ng/L** and a delta of **12 ng/L** to 0h

Greyzone: Patients not identified by both algorithms (elevated but stable TnI values)

3 of 1.045 patients lost to follow-up; median 183 days



Follow-up mortality

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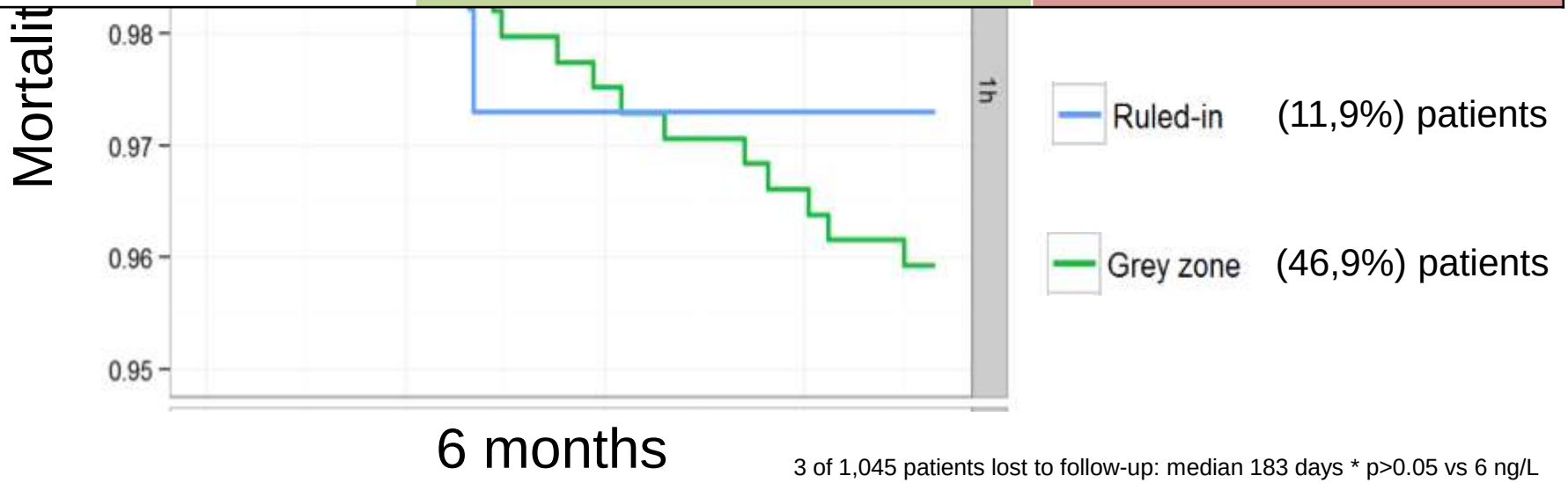
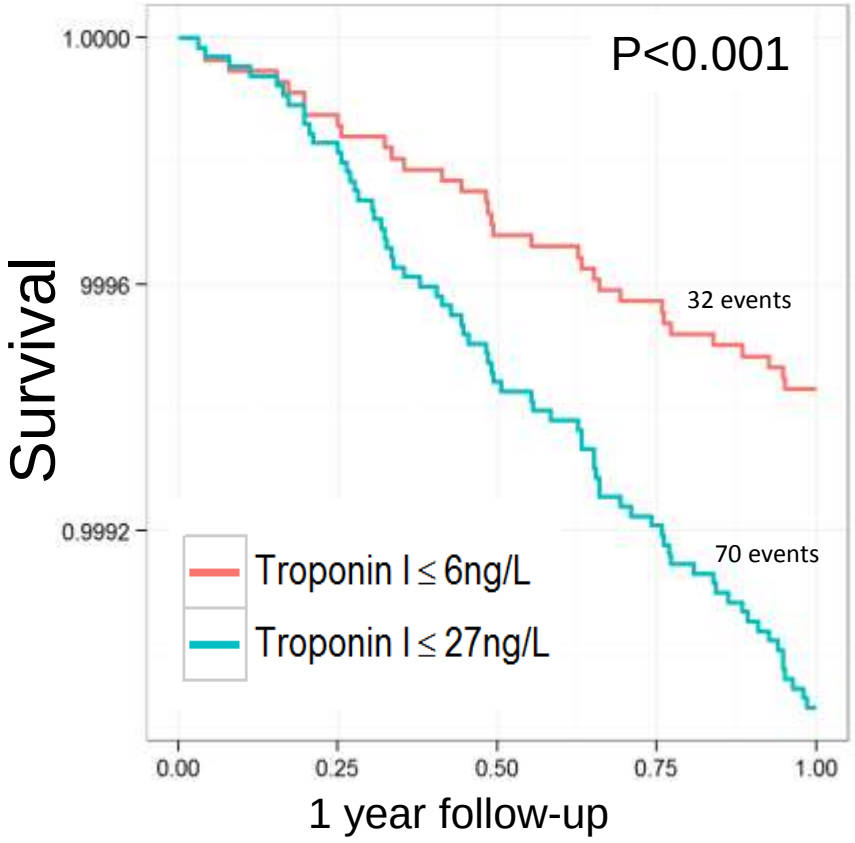
Rule-out	6 ng/L	27 ng/L (99th percentile)
6 months mortality	3 deaths (0.79%)	12 deaths (1.73%) *

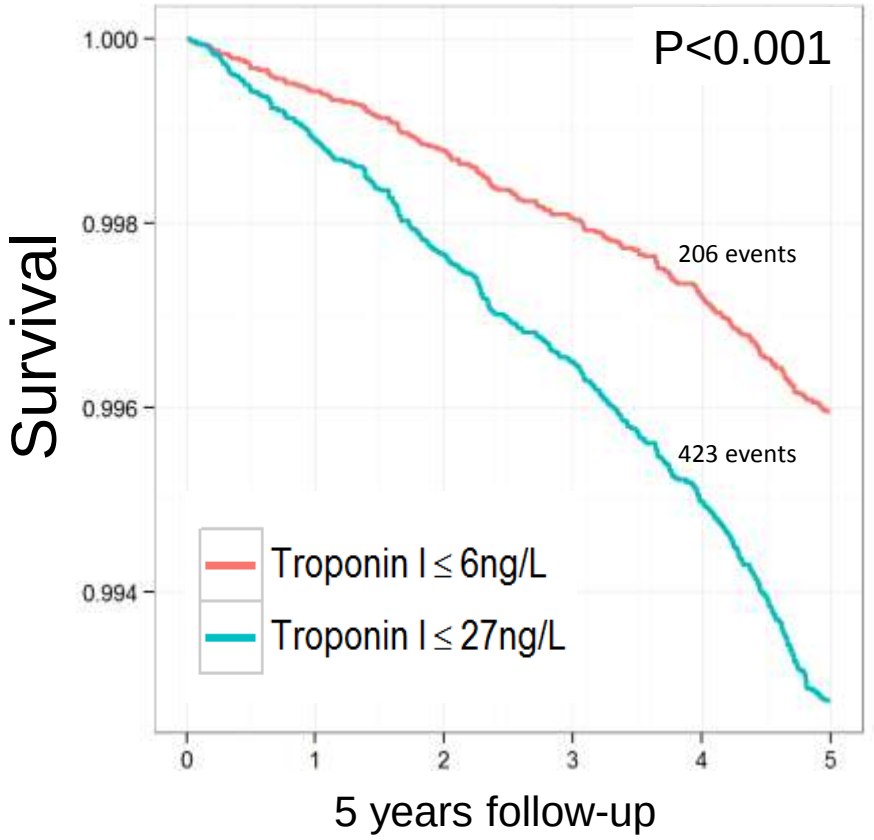


3 of 1,045 patients lost to follow-up: median 183 days * p>0.05 vs 6 ng/L

Follow-up mortality in

74,738 individuals (aged 51.0 years (42-60)) of the general population without prevalent CVD with follow up for cardiovascular mortality.





Conclusion

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- A 1-hour algorithm is safe to rule-out AMI.
- A sensitive troponin I cut-off (6 ng/L) performed better compared to the 99th percentile (27 ng/L) in view of lower follow-up mortality.
- Low troponin I values predict mortality in the general population.
- Further studies are needed to test the best cut-off for each troponin assay and to validate a 1-hour algorithm prospectively.

Prospective **L**ongitudinAl **T**rial of **F**FRCT **O**utcome and **R**esource I**M**pacts

Clinical outcomes of FFRCT-guided diagnostic strategies versus usual care in patients with suspected coronary artery disease

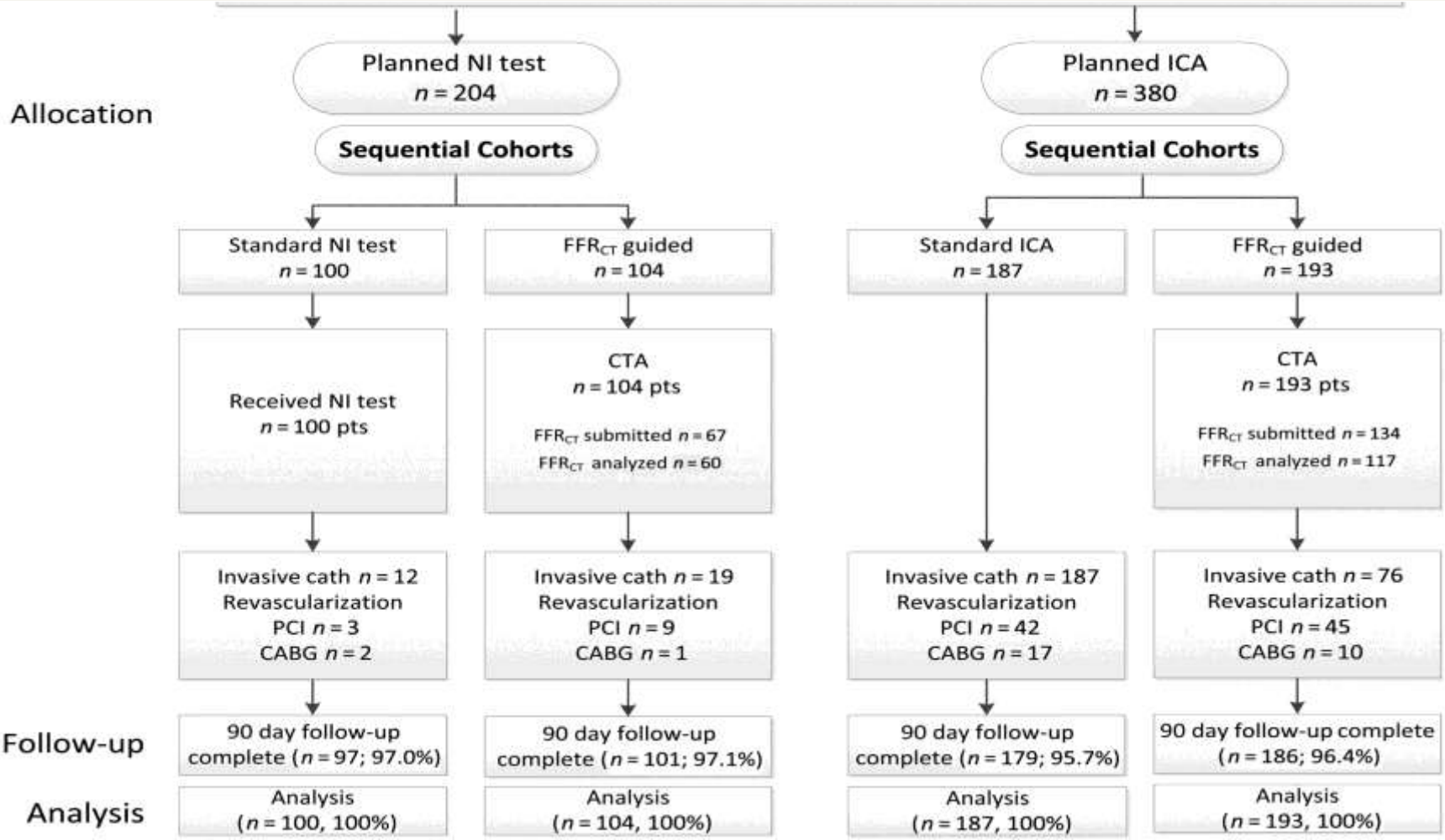
Pamela S. Douglas, Gianluca Pontone, Mark A. Hlatky, Manesh R. Patel, Campbell Rogers, Bernard De Bruyne

Background and Aim

- The optimal evaluation of new onset stable chest pain is uncertain. Ideally, testing will clarify the diagnosis and direct subsequent care while maximizing efficiency and safety.
- The recent PROMISE and SCOT-HEART trials compared anatomic and functional strategies, finding that CTA improved processes of care. However, CTA also increased rates of invasive catheterization and revascularization with no significant reduction in events.
- Fractional Flow Reserve derived from CTA (FFRCT) may address these limitations by providing both functional and anatomic data.
- **STUDY AIM: To determine whether use of a CTA/FFRCT guided strategy, as compared to standard practice, will reduce the rate of invasive angiograms that show no obstructive CAD, without increasing the occurrence of major cardiac events.**

PLATFORM Trial Design

Stable CAD symptoms; Planned non-emergent NI test or catheterization Age ≥ 18y; No prior CAD hx; Intermediate pretest probability of CAD



European Heart Journal

Determination of the rate of invasive catheterization without obstructive coronary artery disease.

CORO d'emblée:

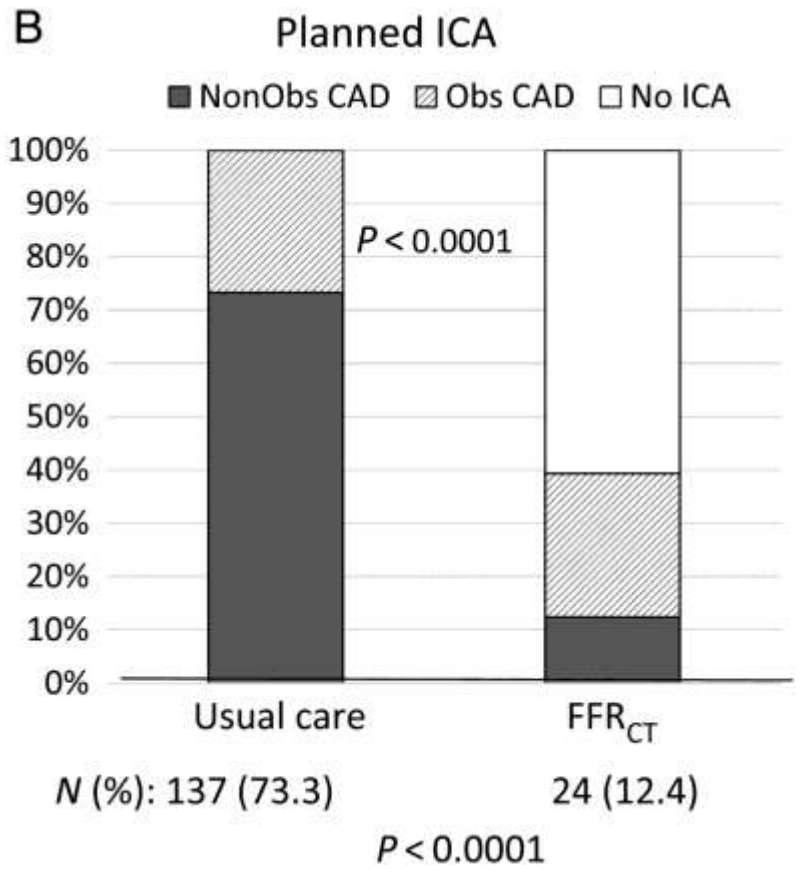
Pas de lésions significatives : 73%

FFR_{ct} :

CORO jugée inutile : 60%

Lx non significatives: 11%

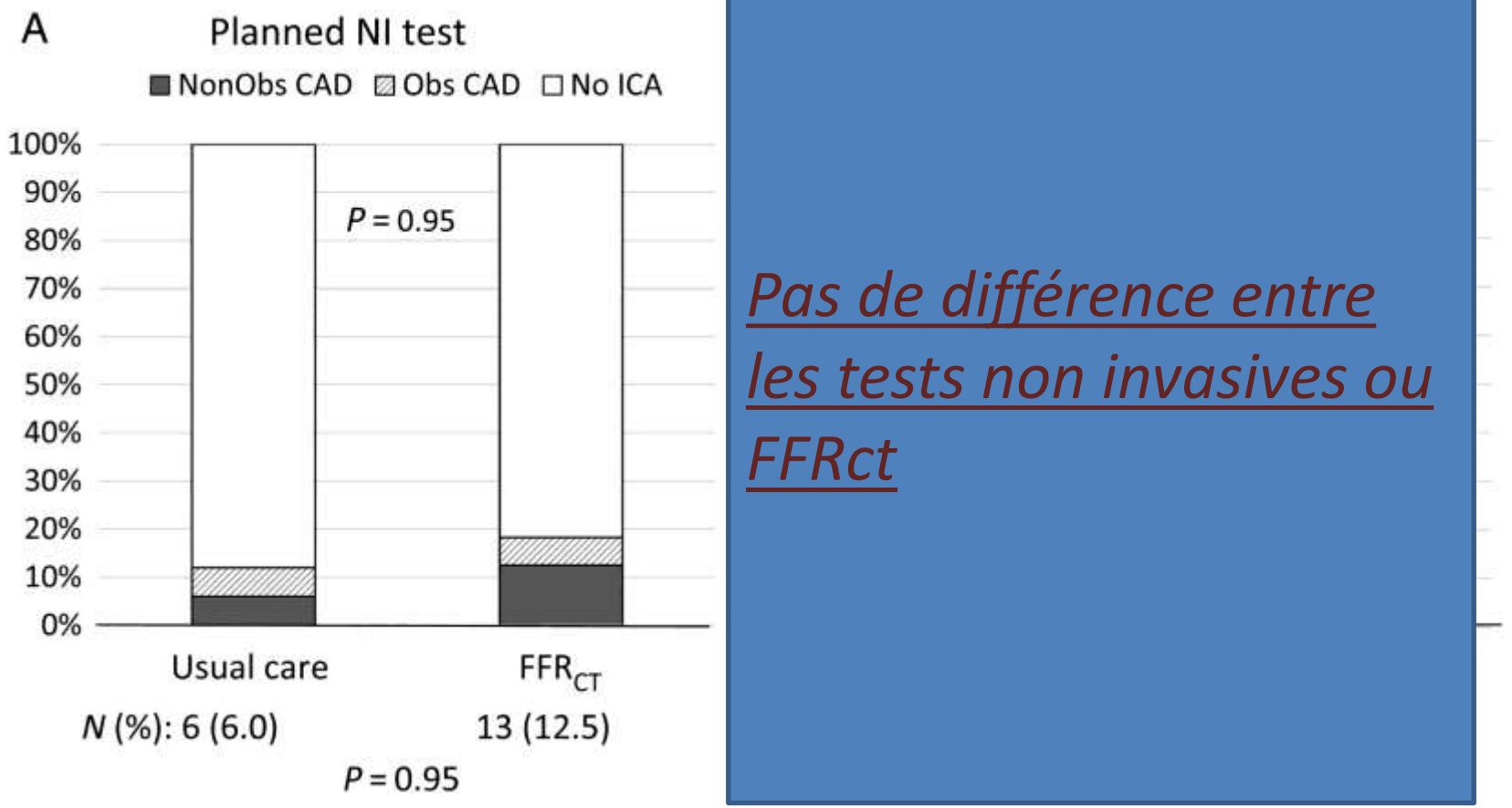
Augmente la rentabilité de la CORO



Pamela S. Douglas et al. Eur Heart J 2015;eurheartj.ehv444

European Heart Journal

Determination of the rate of invasive catheterization without obstructive coronary artery disease.



Pas de différence entre les tests non invasives ou FFRct

Pamela S. Douglas et al. Eur Heart J 2015;eurheartj.ehv444

European Heart Journal

Summary and Conclusion

- No differences in MACE, radiation or revascularization rates

- En Conclusion :

  - Le Coro Scanner avec étude de la FFR permet de trier les patients et de reduire l'utilisation du test invasif

  - Il faut envisager d' inclure ce test dans la stratégie diagnostique

ALBATROSS

Aldosterone **L**ethal effects **B**lockade in **A**cute myocardial infarction **T**reated with or without **R**eperfusion to improve **O**utcome and **S**urvival at **S**ix months follow-up

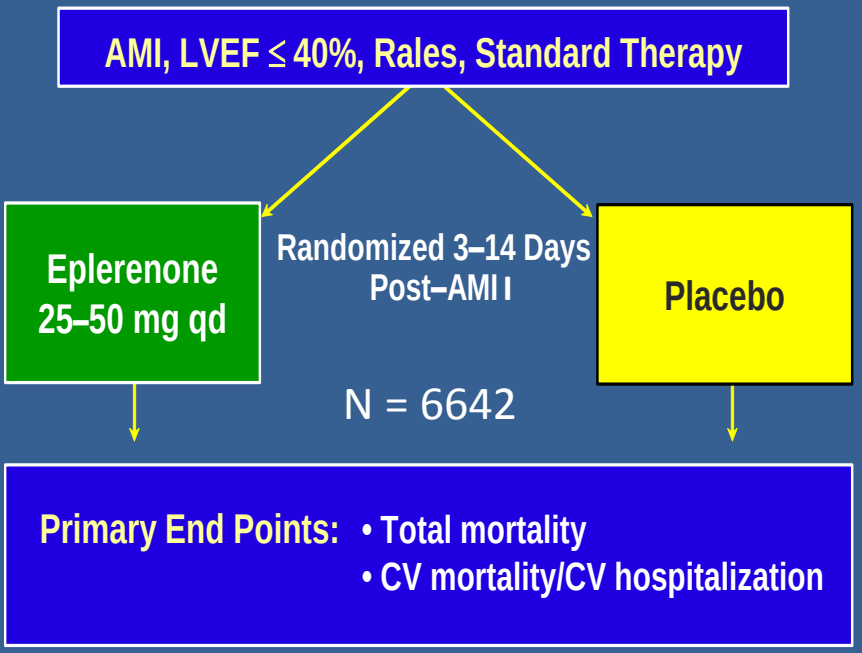
F. Beygui, G. Cayla, V. Roule, F. Roubille, N. Delarche, J. Silvain, E. Van Belle, L. Belle, M. Galinier, P. Motreff, L. Cornillet, JP Collet, A. Furber, P. Goldstein, P. Ecollan, D. Legallois, A. Lebon, H. Rousseau, J. Machecourt, F. Zannad, E. Vicaut, G. Montalescot

on behalf of the ALBATROSS investigators

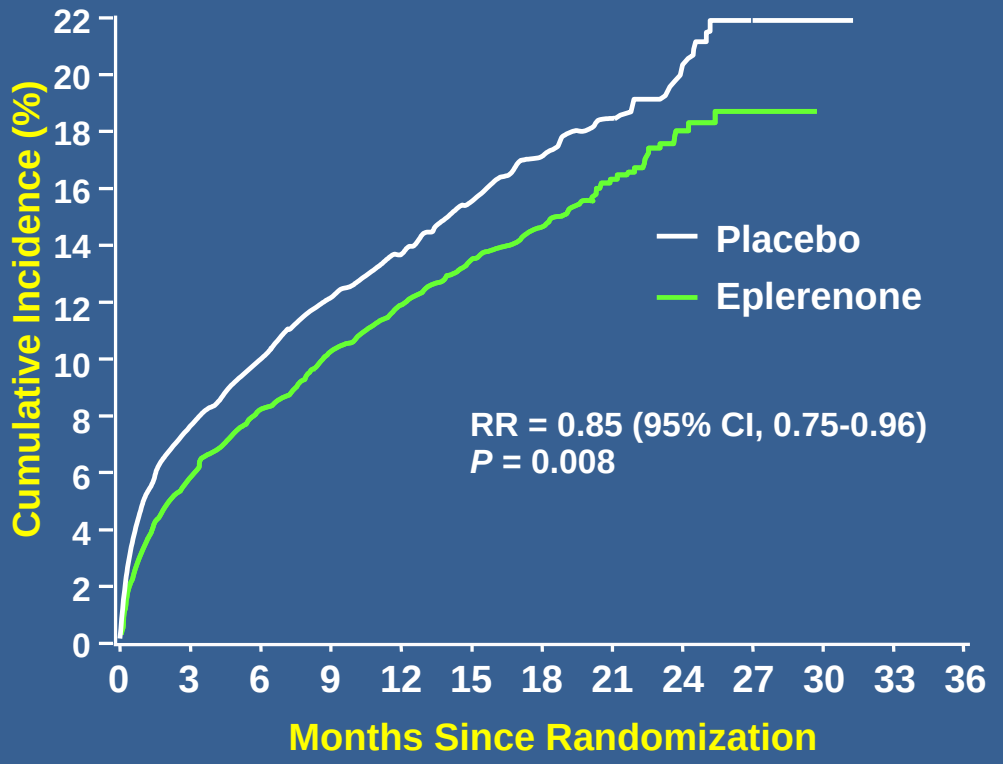
COI Disclosure for Dr. Montalescot: **Research Grants to the Institution or Consulting/Lecture Fees** from Abbott Vascular, Astra-Zeneca, Bayer, Biotronik, Boehringer-Ingelheim, Boston Scientific, Cleveland Clinic Foundation, Cardiovascular Research Foundation, Cordis, Daiichi-Sankyo, Duke institute, Eli-Lilly, Europa, Fédération Française de Cardiologie, Fondation de France, GSK, ICM, INSERM, Medtronic, Menarini, Nanospheres, Novartis, Pfizer, Sanofi-Aventis Group, Servier, Société Française de Cardiologie, The Medicines Company, TIMI group.

EPHESUS : Post-MI heart failure

Design

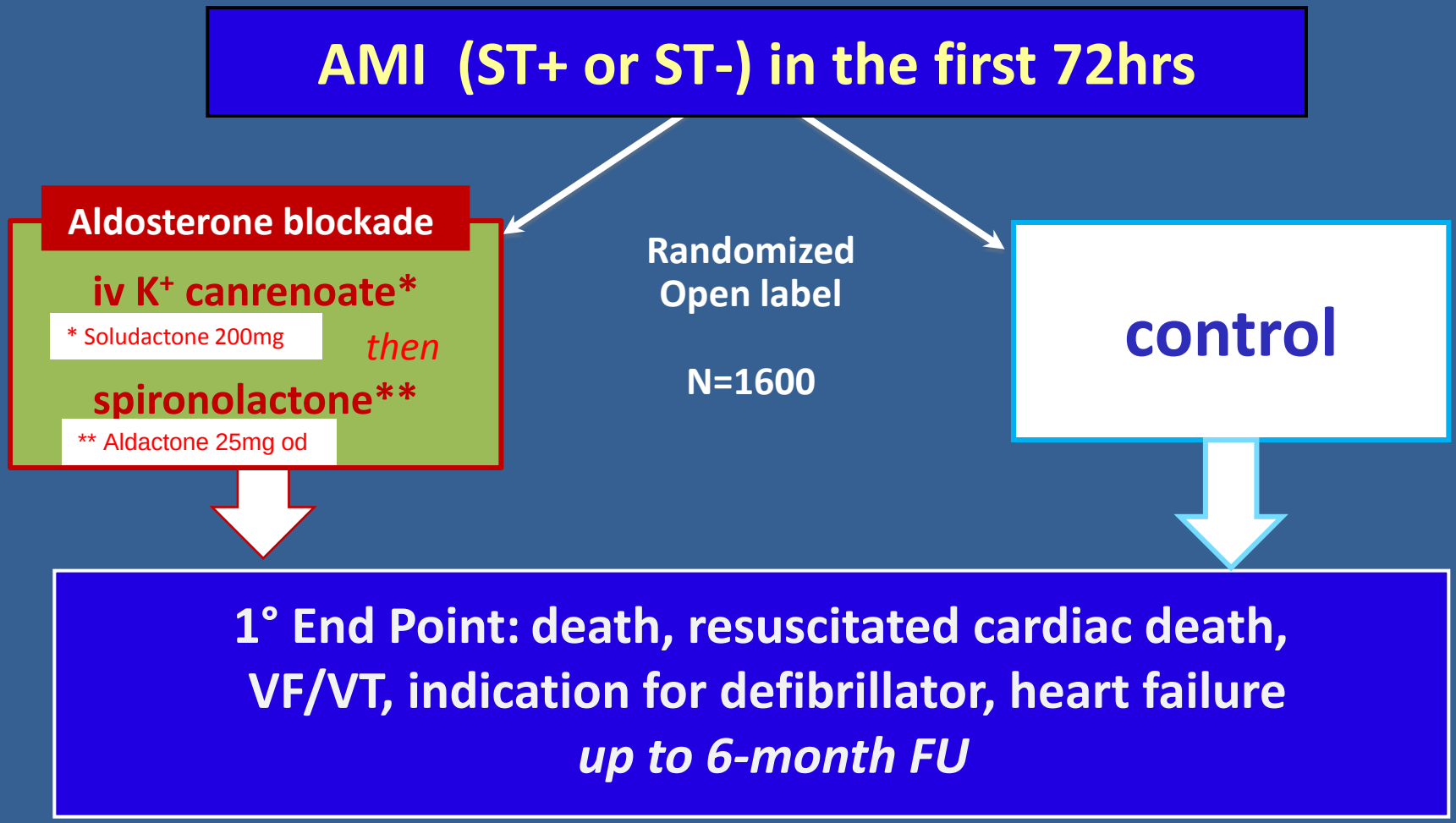


Mortality



Pitt B, et al. *New Engl J Med.* 2003; 348:1309-21.

ALBATROSS study design



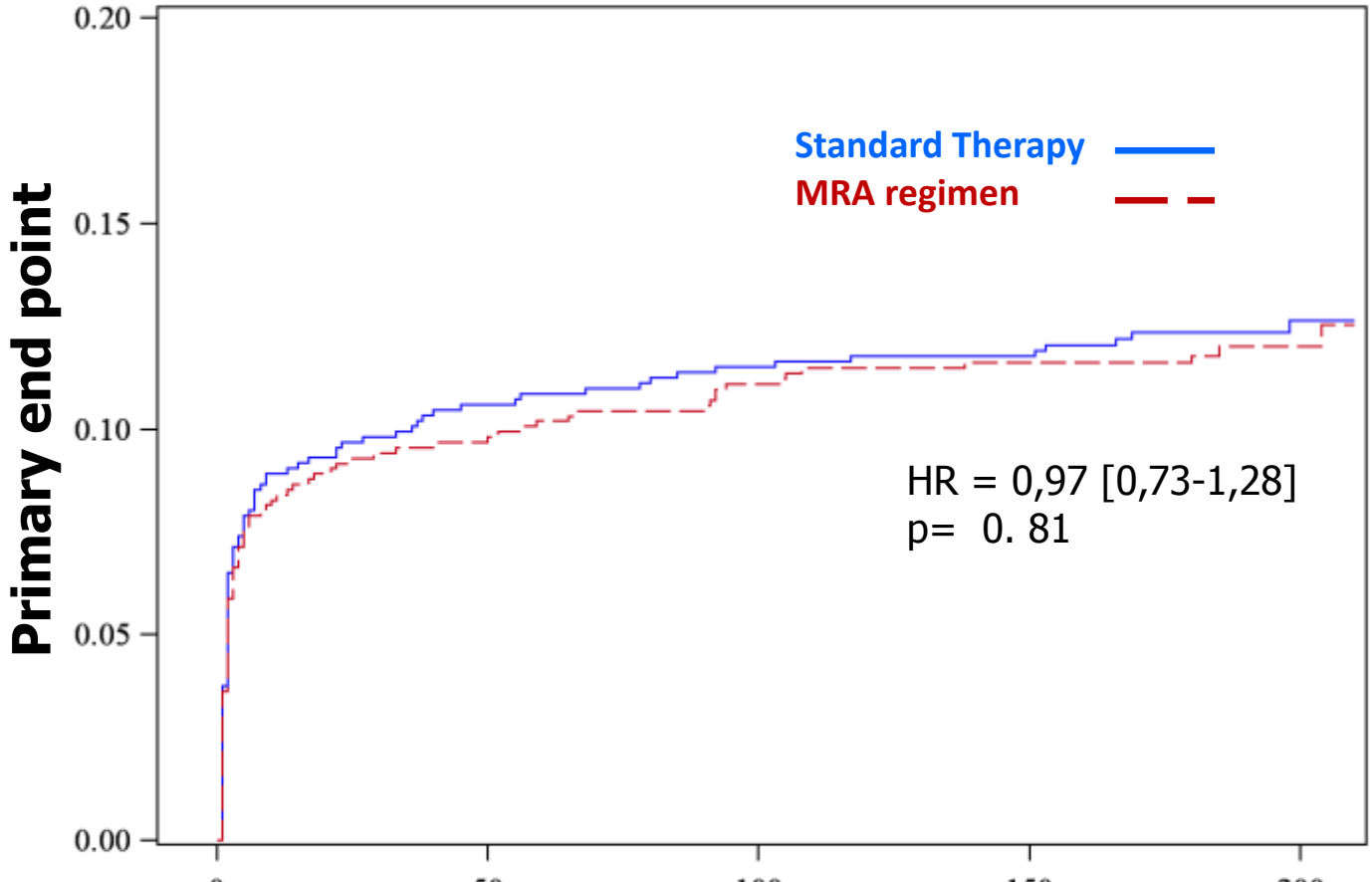
clinicaltrials.gov registration number NCT 01059136
ALBATROSS study protocol - Beygui et al. Am Heart J 2010

Baseline characteristics

	Standard treatment (N=801)	MRA regimen (N=802)
Age (median)	58	58
Current smoking (%)	52	47
Diabetes (%)	16	16
Hypertension (%)	44	42
Dyslipidemia (%)	46	47
Prior MI (%)	9	8
Prior HF (%)	1	1
STEMI (n)	617	612
NSTEMI (n)	183	186
Killip I (%)	91	93
PCI (%)	81	82
LV ejection fraction (median in %)	50	50

Primary End Point

Death, resuscitated death, VF/VT, indication for ICD *or* heart failure



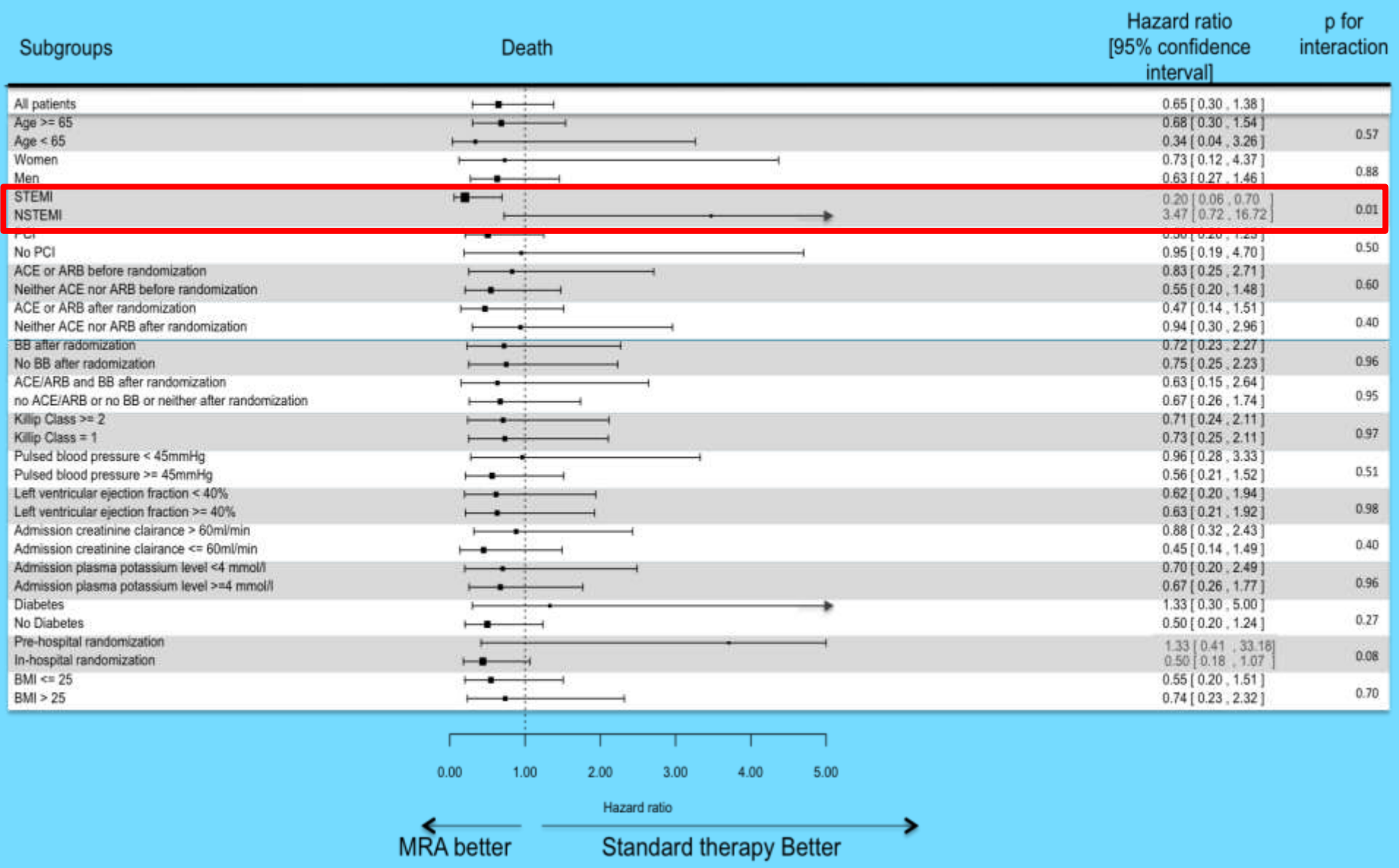
N at risks					
Standard Therapy	801	687	669	645	273
MRA Regimen	802	705	683	660	183

MRA: Mineralocorticoid Receptor Antagonist; VF: Ventricular Fibrillation; VT: Ventricular Tachycardia; ICD: Implantable Cardioverter Defibrillator

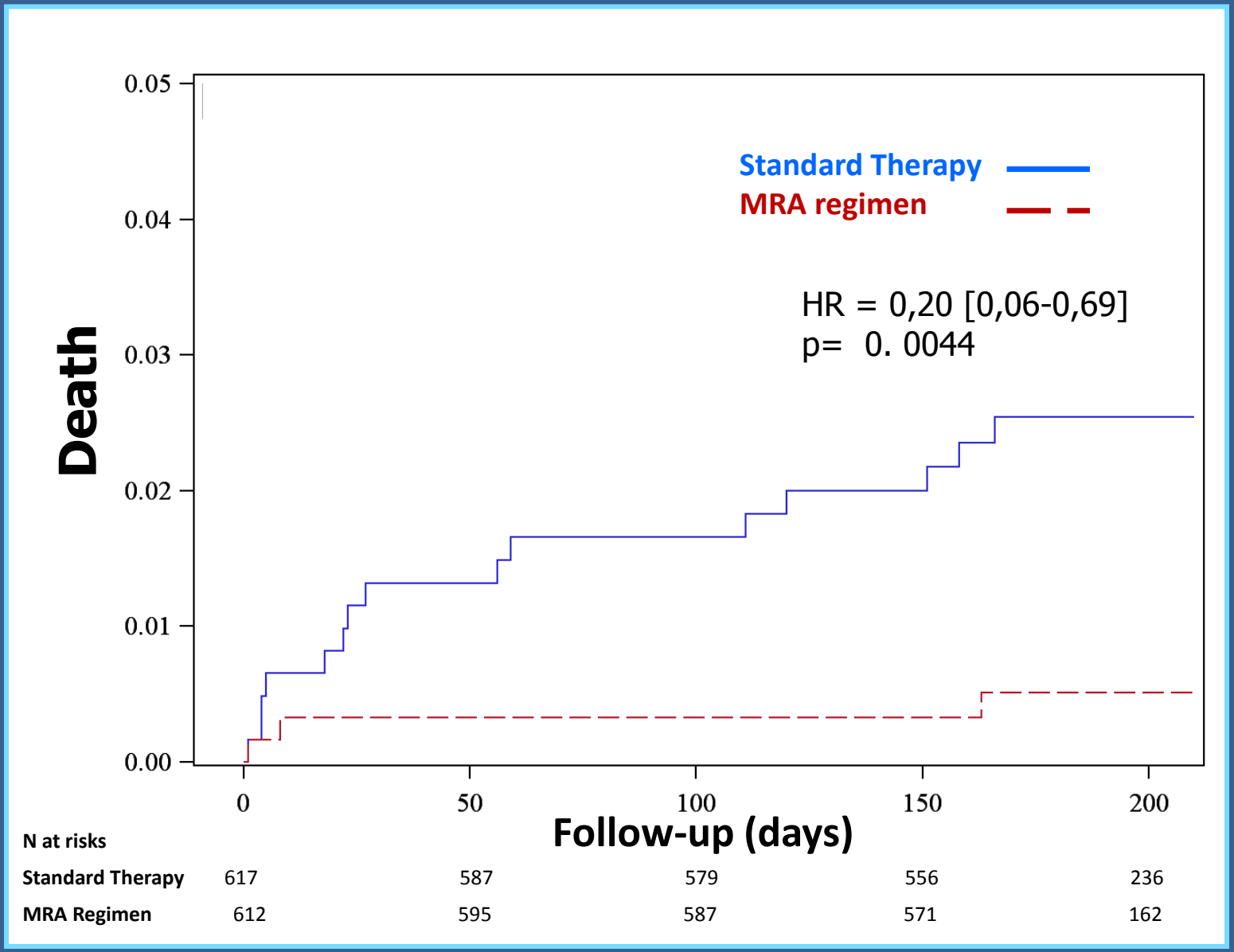
Secondary End Points

	Standard therapy (n=801)	MRA regimen (n=802)	P value
Significant ventricular arrhythmia (%)	6	5.6	0.75
New or worsening heart failure (%)	5.6	5.9	0.85
Recurrent myocardial infarction (%)	1	0.6	0.39
Death or resuscitated cardiac arrest (%)	2.4	1.6	0.28
Hyperkalemia > 5.5mmol.L^{-1} (%)	**0.2**	**3**	**<0.0001**

Death in pre-specified subgroups



Death in STEMI patients (n=1229)



1. Despite a strong pre-clinical rationale and favorable clinical data from registries and small randomized studies, the ALBATROSS trial failed to show a benefit of aldosterone blockade initiated early in MI, when heart failure is in general not present

2. Our finding of a mortality reduction associated with early aldosterone blockade in STEMI patients needs confirmation in future studies specifically dedicated to these patients

1. Meanwhile, the results of the ALBATROSS study do not warrant the extension of aldosterone blockade to MI patients without heart failure.

Rationale and design of the Cyclosporine to ImpRove Clinical oUtcome in ST-elevation myocardial infarction patients (the CIRCUS trial)

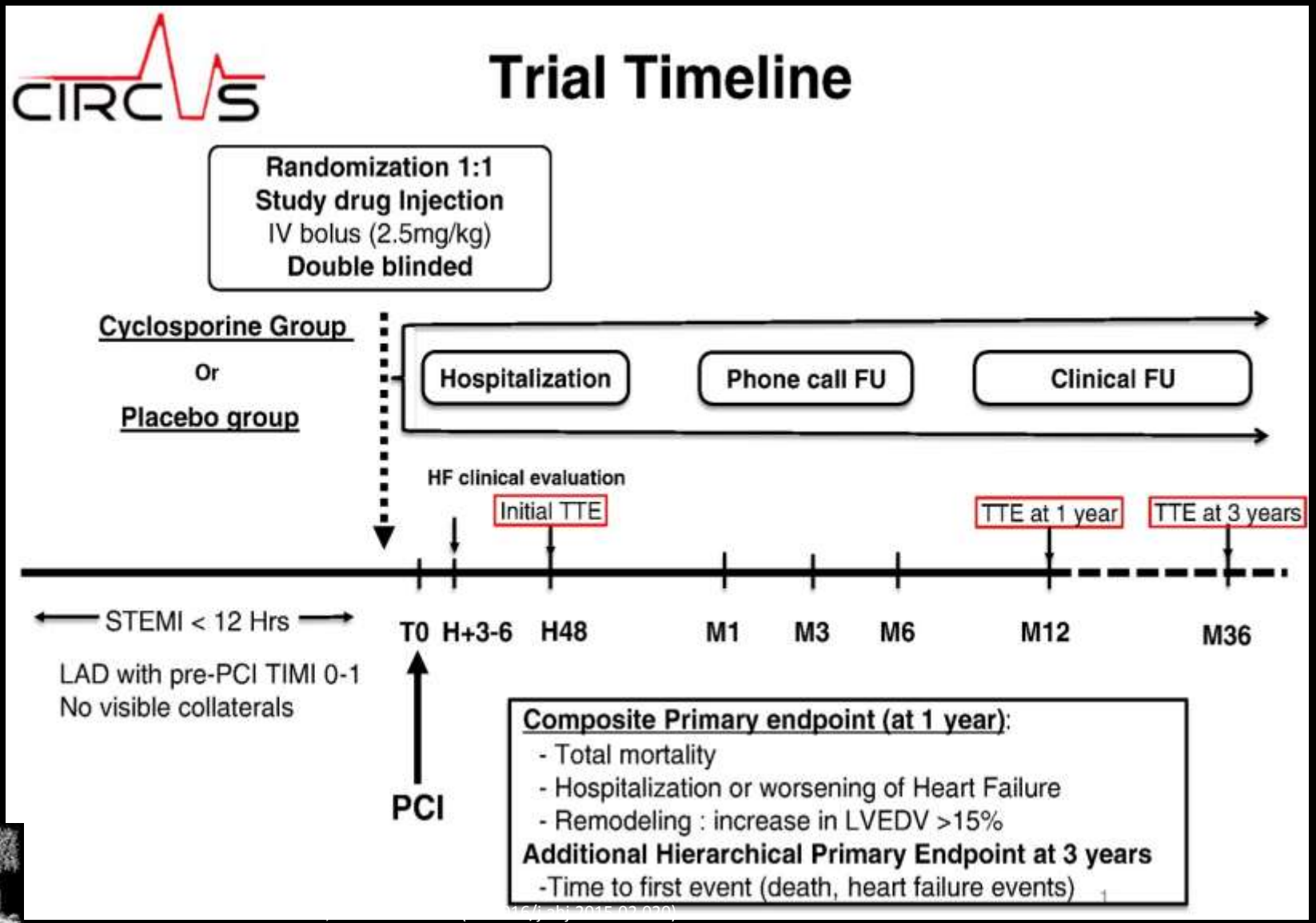
Nathan Mewton, MD, PhD, Thien T. Cung, MD, Olivier Morel, MD, PhD, Guillaume Cayla, MD, PhD, Eric Bonnefoy-Cudraz, MD, PhD, Gilles Rioufol, MD, PhD, Denis Angoulvant, MD, PhD, Patrice Guerin, MD, PhD, Meyer Elbaz, MD, PhD, Nicolas Delarche, MD, Pierre Coste, MD, PhD, Gerald Vanzetto, MD, PhD, Marc Metge, MD, Jean-François Aupetit, MD, Bernard Jouve, MD, Pascal Motreff, MD, PhD, Christophe Tron, MD, Jean-Noël Labeque, MD, Pierre G. Steg, MD, PhD, Yves Cottin, MD, PhD, Grégoire Range, MD, Jerome Clerc, MD, Patrick Coussement, MD, Fabrice Prunier, MD, PhD, Frederique Moulin, MD, Olivier Roth, MD, Loic Belle, MD, Phillipe Dubois, MD, Paul Barragan, MD, Martine Gilard, MD, PhD, Christophe Piot, MD, PhD, Patrice Colin, MD, Marie-Claude Morice, MD, Jean-Pierre Monassier, MD, Omar Ider, MD, Jean Luc P. Dubois-Randé, MD, PhD, Thierry Unterseeh, MD, Hervé Lebreton, MD, PhD, Thierry Beard, MD, Didier Blanchard, MD, Gilles Grollier, MD, Vincent Malquarti, MD, Patrick Staat, MD, Arnaud Sudre, MD, Magnus J. Hansson, MD, Eskil Elmer, PhD, Inesse Boussaha, MSc, Claire Jossan, MSc, Anna Torner, Marc Claeys, MD, PhD, David Garcia-Dorado, MD, PhD, Michel Ovize, MD, PhD

American Heart Journal
Volume 169, Issue 6, Pages 758-766.e6 (June 2015)
DOI: 10.1016/j.ahj.2015.02.020

Objectif de l etude

Démontrer que la Cyclosporine permet de prevenir les lesions de reperfusion lorsqu' elle est donnée juste avant l' ouveture des coronaires par angioplastie chez les patients avec IDM ST+

Etude multicentrique : 42centres
970 patients sont inclus



Characteristics of the Patients at Baseline.

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Cyclosporine (N=474)	Control (N=495)
Age — yr	60.4±13.1	59.5±12.7
Male sex — no. (%)	399 (84.2)	396 (80.0)
Body-mass index†	26.9±4.3	26.8±4.1
Killip class at admission — no./total no. (%)		
I	369/422 (87.4)	381/437 (87.2)
II	45/422 (10.7)	41/437 (9.4)
III	6/422 (1.4)	10/437 (2.3)
IV	2/422 (0.5)	5/437 (1.1)
Current smoking — no. (%)	185 (39.0)	226 (45.7)
Hypertension — no. (%)	178 (37.6)	183 (37.0)
Diabetes mellitus — no. (%)	65 (13.7)	58 (11.7)
Dyslipidemia — no. (%)	186 (39.2)	187 (37.8)
Previous myocardial infarction — no. (%)	28 (5.9)	26 (5.3)
Previous ischemic heart disease — no. (%)	31 (6.5)	32 (6.5)
Treated with CABG — no./total no. (%)	1/31 (3.2)	0/32
Treated with PCI — no./total no. (%)	26/31 (83.9)	25/32 (78.1)
Managed medically — no./total no. (%)	4/31 (12.9)	7/32 (21.9)
Previous heart failure — no. (%)	1 (0.2)	5 (1.0)

* Plus–minus values are means ±SD. There were no significant between-group differences in any of the characteristics listed, except for current smoking (P=0.03). CABG denotes coronary-artery bypass grafting, and PCI percutaneous coronary intervention.

† The body-mass index is the weight in kilograms divided by the square of the height in meters.

Procedural Characteristics.

Table 2. Procedural Characteristics.*

Characteristic	Cyclosporine (N = 474)	Control (N = 495)
Time from symptom onset to hospital arrival — hr	3.4±3.0	3.4±3.1
Time from hospital arrival to treatment administration — hr	1.0±1.3	1.1±1.7
Total ischemic time		
Duration — hr†	4.4±3.0	4.5±2.9
Distribution — no./total no. (%)		
<2 hr	54/432 (12.5)	42/446 (9.4)
2–6 hr	306/432 (70.8)	307/446 (68.8)
>6 hr	72/432 (16.7)	97/446 (21.7)
Prehospital thrombolysis — no./total no. (%)	28/474 (5.9)	32/493 (6.5)
Medication from first medical care to PCI — no./total no. (%)‡		
Heparin	388/474 (81.9)	408/493 (82.8)
Glycoprotein IIb/IIIa inhibitor	181/474 (38.2)	185/493 (37.5)
Loading dose of $P2Y_{12}$ inhibitor	428/474 (90.3)	435/493 (88.2)
Aspirin	445/474 (93.9)	453/493 (91.9)
Morphine	284/474 (59.9)	270/493 (54.8)
Site of occlusion in left anterior descending artery — no. (%)		
Proximal or main left artery	214 (45.1)	203 (41.0)
Medial or distal segment or diagonal branch	260 (54.9)	292 (59.0)
Multivessel disease — no. (%)	194 (40.9)	164 (33.1)
Thrombus burden ≥3 — no./total no. (%)	311/447 (69.6)	315/483 (65.2)
Rentrop score of 2 or 3 — no./total no. (%)§	29/446 (6.5)	36/483 (7.5)
Area at risk — %¶	36.5±8.4	36.1±8.6
TIMI flow grade before PCI — no./total no. (%)‖		
0	359/446 (80.5)	395/483 (81.8)
1	55/446 (12.3)	55/483 (11.4)
2	21/446 (4.7)	27/483 (5.6)
3	11/446 (2.5)	6/483 (1.2)
Thrombus aspiration — no. (%)	359 (75.7)	377 (76.2)
Stenting — no. (%)	422 (89.0)	434 (87.7)
No reflow observed on angiography — no. (%)	27 (5.7)	28 (5.7)
TIMI flow grade after PCI — no./total no. (%)		
0	6/466 (1.3)	7/487 (1.4)
1	5/466 (1.1)	5/487 (1.0)
2	33/466 (7.0)	25/487 (5.1)
3	422/466 (90.6)	450/487 (92.4)

* Plus–minus values are means ±SD. There were no significant between-group differences in any of the characteristics listed, except for multivessel disease (P = 0.01). TIMI denotes Thrombolysis in Myocardial Infarction.

† Data were missing for 42 patients in the cyclosporine group and for 49 in the control group.

‡ Heparin was low-molecular-weight heparin or unfractionated heparin. $P2Y_{12}$ inhibitors included clopidogrel, prasugrel, and ticagrelor.

§ Scores on the Rentrop classification range from 0 to 3, with higher scores indicating greater degree of collateral circulation. A score of 0 indicates no filling of any collateral channels; 1, filling of side branches of the artery to be perfused by collateral vessels without visualization of the epicardial segment; 2, partial filling of the epicardial artery by collateral vessels; and 3, complete filling of the epicardial artery by collateral vessels. Local investigators could not always accurately assess Rentrop scores in emergency settings, so some patients with a Rentrop score of 2 or 3 were included in the trial. This situation was corrected at the end of the trial by the centralized, blinded analysis and was taken into account by the per-protocol analysis.

¶ The area at risk was assessed by means of the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH) score.[16] The APPROACH score is a scoring system in which the left ventricle is divided into regions defined by the distribution of perfusion of each coronary artery, and the estimated amount of myocardium in each region is used to calculate the amount of jeopardized myocardium for a given site of vessel occlusion. The area at risk is expressed as the percent of the left ventricular mass.

‖ Some patients with a TIMI flow grade of 2 or 3 were included by local investigators, which was a protocol deviation. All coronary angiograms were read centrally by persons who were unaware of the study-group assignments, and the situation was taken into account in the per-protocol analysis.

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Primary and secondary outcomes at 1 year

	Cyclosporine (n=395)	Control (n=396)	Odds Ratio (95% CI)	P value
(Death / HF / LV remodeling)	233 (**59.0 %**)	230 (**58.1%**)	1.04 [0.78; 1.39]	0.77
Death: all-cause	7.1 %	6.6 %	1.09 [0.63 ; 1.90]	0.76
Death: cardiovascular	6.1 %	6.1 %	1.01 [0.56 ; 1.81]	0.98
HF worsening or re-hospitalization for HF	22.8 %	22.7 %	1.01 [0.72 ; 1.41]	0.97
HF worsening	15.7 %	16.9 %	0.92 [0.63 ; 1.34]	0.65
Re-hospitalization for HF	10.6 %	10.4 %	1.03 [0.65 ; 1.63]	0.89
LV remodeling	42.8 %	40.7 %	1.09 [0.82 ; 1.46]	0.53
Cardiogenic shock	6.6 %	6.1 %	1.09 [0.61 ; 1.94]	0.77
Recurrent Myocardial infarction	2.3 %	3.8 %	0.59 [0.26 ; 1.37]	0.22
Stroke	1.8 %	3.0 %	0.58 [0.22 ; 1.48]	0.25
Major bleeding	1.8 %	2.3 %	0.73 [0.27 ; 2.00]	0.54

Conclusions

- L administration de la Ciclosporine juste avant l ‘ angioplastie pour IDM ST+ n’améliore pas le pronostic clinique à 1an
- Les lesions de reperfusion : reel problème
- D ‘autres études avec d’ autres molécules sont en cours

LEADLESS II

Percutaneous Implantation of an Entirely Intracardiac Leadless Pacemaker

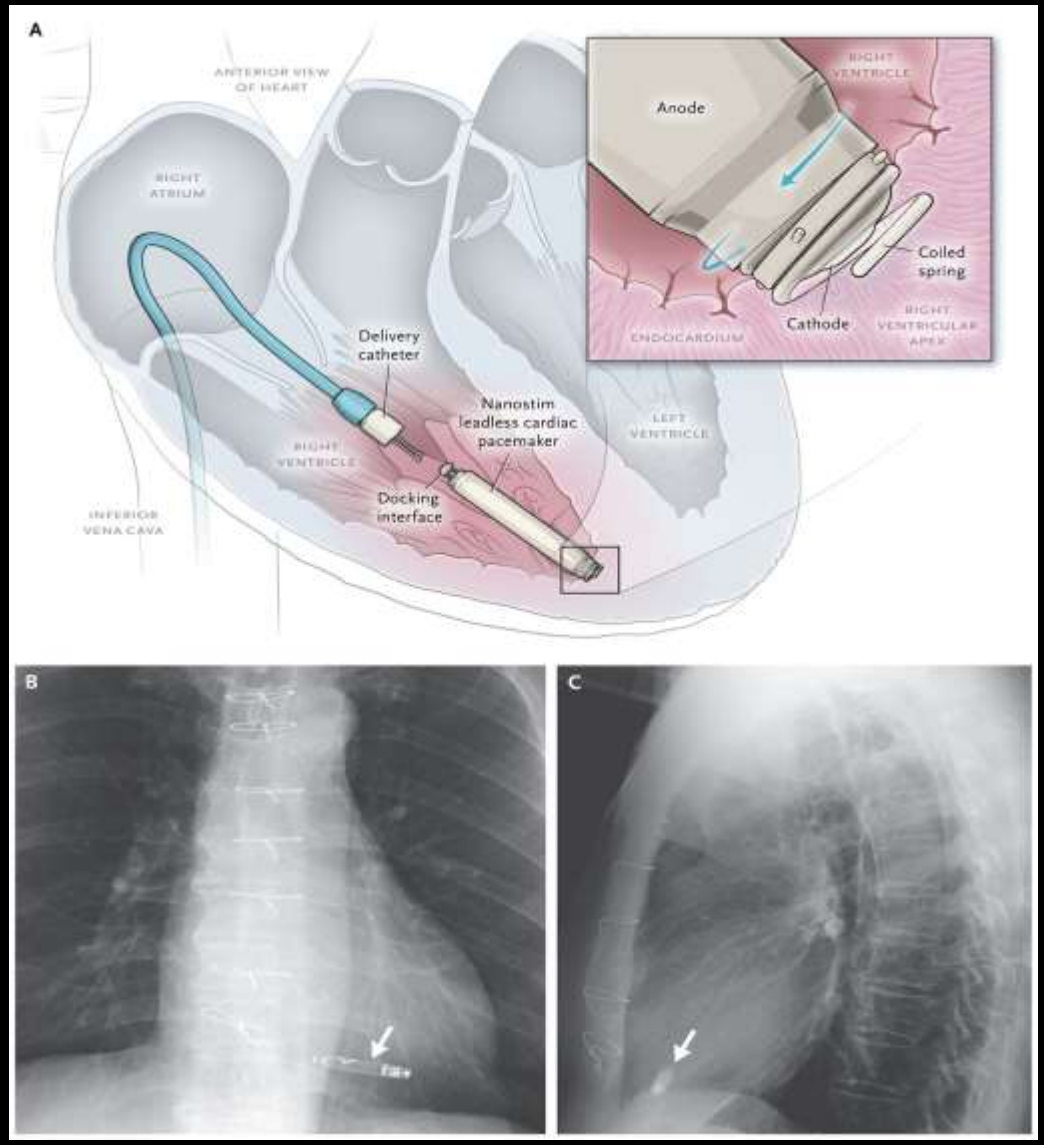
Vivek Y. Reddy, M.D., Derek V. Exner, M.D., M.P.H., Daniel J. Cantillon, M.D., Rahul Doshi, M.D., T. Jared Bunch, M.D., Gery F. Tomassoni, M.D., Paul A. Friedman, M.D., N.A. Mark Estes, III, M.D., John Ip, M.D., Imran Niazi, M.D., Kenneth Plunkitt, M.D., Rajesh Banker, M.D., James Porterfield, M.D., James E. Ip, M.D., Srinivas R. Dukkipati, M.D., for the LEADLESS II Study Investigators

N Engl J Med
Volume 373(12):1125-1135
September 17, 2015

The NEW ENGLAND JOURNAL of MEDICINE

Nanostim*
St Jude

Longueur: 3,8 cm
Diametre: 6 mm



Reddy VY et al. N Engl J Med 2015;373:1125-1135

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Study Overview

- Etude prospective non randomisée
- Etude multicentrique : 56 centres (Etat unies , Canada, Australie)
- 526 patients; de Février 2014 à Juin 2015
- Among the first 300 patients who were followed for 6 months, the pacemaker met prespecified sensing and pacing requirements in 90%, and serious adverse events were observed in 6.7%.

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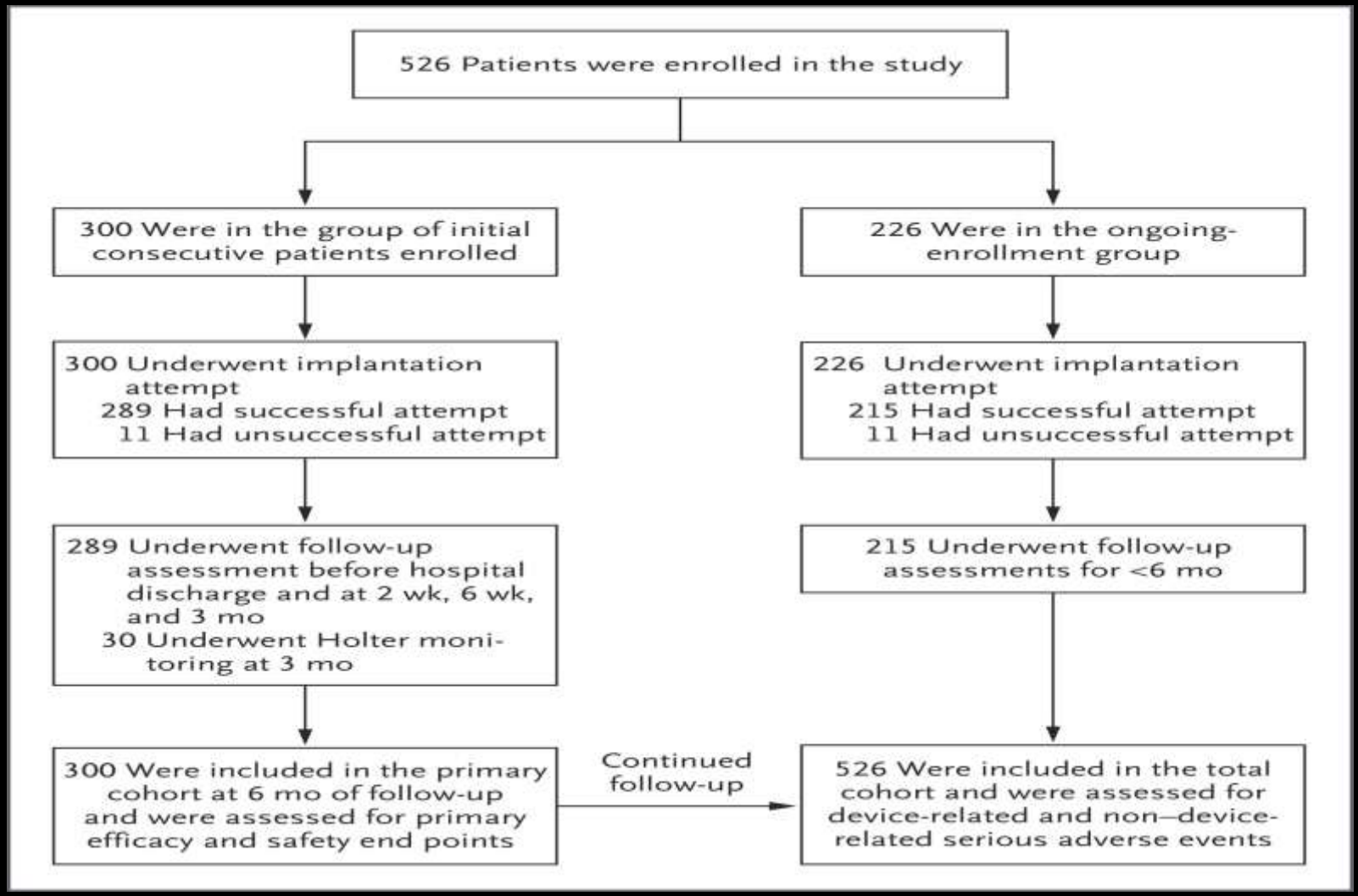
Enrollment, Study Intervention, and Follow-up.



Reddy VY et al. N Engl J Med 2015;373:1125-1135

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Critère Primaire: Critère composite d' efficacité et de sécurité à 6 mois de suivi

Critère laire d'efficacité :

- Seuil de stimulation acceptable (<0,2 v à 0,4 ms)
- Amplitude de détection acceptable (Onde R>5 mV)

Critère laire de sécurité :

- Absence d' événements indésirables graves liés au dispositif

Resultats

Après 6 mois l étude a répondu aux deux critères d’ évaluation

- Efficacité : Critère atteint chez 90% de la 1 ère cohorte (270/300)

- Sécurité : Critère obtenu dans 93,3% (280/300)

Reddy VY et al. N Engl J Med 2015;373:1125-1135

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Evenements graves liés au dispositif

Table 2. Device-Related Serious Adverse Events.*

Event	Primary Cohort (N = 300)			Total Cohort (N = 526)		
	No. of Events	No. of Patients	Event Rate	No. of Events	No. of Patients	Event Rate
			%			%
Total	22	20	6.7	40	34	6.5
Cardiac perforation						
Cardiac tamponade with intervention	1	1	0.3	5	5	1.0
Cardiac perforation requiring intervention	1	1	0.3	1	1	0.2
Pericardial effusion with no intervention	2	2	0.7	2	2	0.4
Vascular complication						
Bleeding	2	2	0.7	2	2	0.4
Arteriovenous fistula	1	1	0.3	1	1	0.2
Pseudoaneurysm	1	1	0.3	2	2	0.4
Failure of vascular closure device requiring intervention	0	0	0	1	1	0.2
Arrhythmia during device implantation						
Asystole	1	1	0.3	1	1	0.2
Ventricular tachycardia or ventricular fibrillation	1	1	0.3	2	2	0.4
Cardiopulmonary arrest during implantation procedure	0	0	0	1	1	0.2
Device dislodgement	5	5	1.7	6	6	1.1
Device migration during implantation owing to inadequate fixation	0	0	0	2	2	0.4
Pacing threshold elevation with retrieval and implantation of new device	4	4	1.3	4	4	0.8
Other						
Hemothorax	0	0	0	1	1	0.2
Angina pectoris	0	0	0	1	1	0.2
Pericarditis	1	1	0.3	1	1	0.2
Acute confusion and expressive aphasia	0	0	0	1	1	0.2
Dysarthria and lethargy after implantation	0	0	0	1	1	0.2
Contrast-induced nephropathy	0	0	0	1	1	0.2
Orthostatic hypotension with weakness	1	1	0.3	1	1	0.2
Left-leg weakness during implantation	0	0	0	1	1	0.2
Probable pulmonary embolism	1	1	0.3	1	1	0.2
Ischemic stroke	0	0	0	1	1	0.2

* Events were classified as device-related if they were considered by the clinical-events committee to be attributable to the investigational device or procedure. Some patients had more than one event, and therefore the number of patients is less than the number of events.

Reddy VY et al. N Engl J Med 2015;373:1125-1135

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Resultats

Après 6 mois l étude a répondu aux deux critères d' évaluation

- Efficacité : Critère atteint chez 90% de la 1 ère cohorte (270/300)

- Sécurité : Critère obtenu dans 93,3% (280/300)

Dans la cohorte totale :

- Durée de la procédure : 28,6 ± 17 min
- Succès d' implantation : 95,8 % (504/526)
- Mortalité : 28 (5,3%)
- Extraction du dispositif possible dans 100%
- Longévité de l appareil : 9,8 années

Reddy VY et al. N Engl J Med 2015;373:1125-1135

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Conclusions

Le stimulateur Nanostim* répond aux deux criteres d éfficacité et de sécurité à 6 mois

Option minimalement invasive et sans sonde pour la stimulation ventriculaire simple chambe

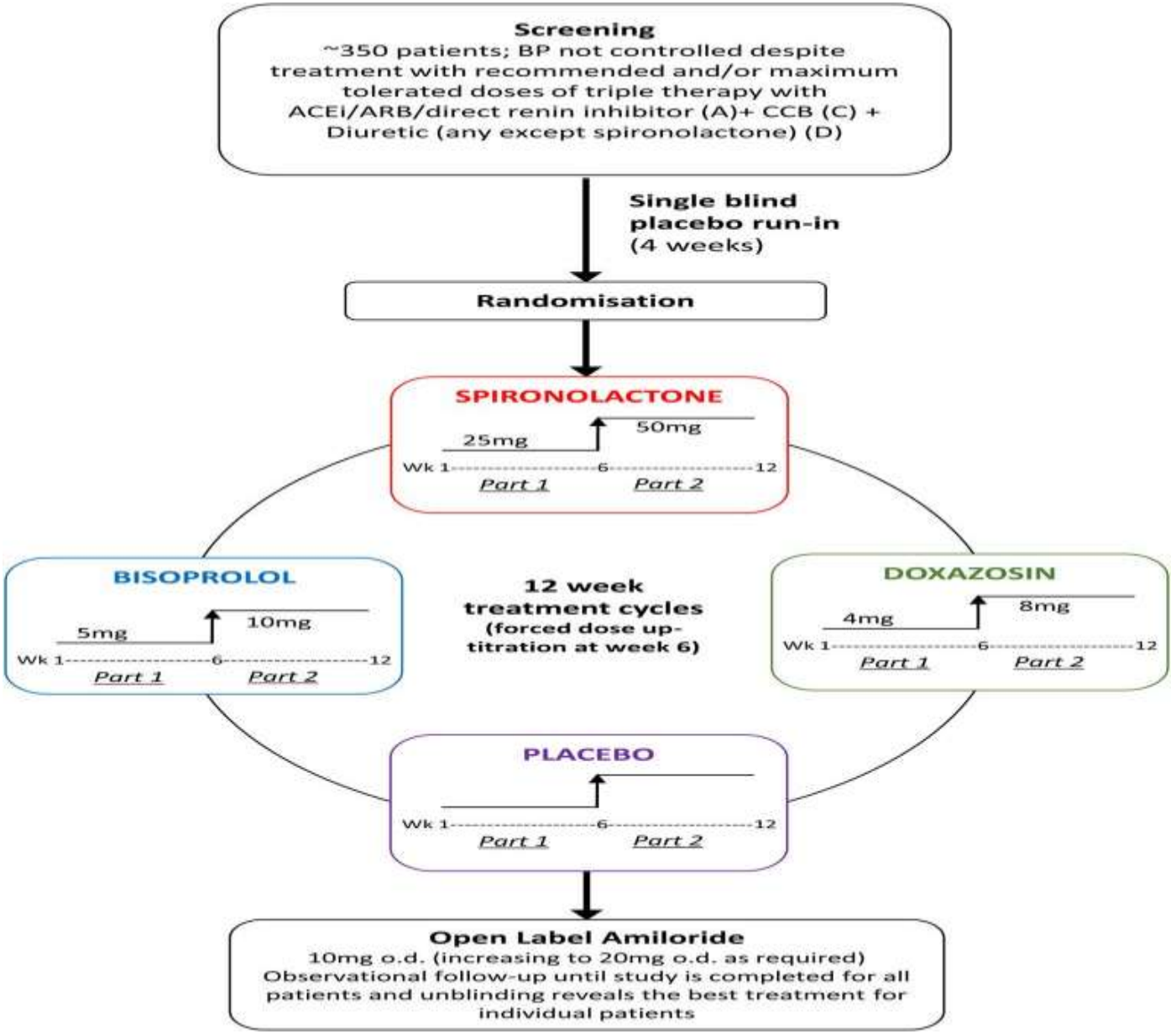
Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension (PATHWAY-2): a randomised, double-blind, crossover trial

Bryan Williams, ProfFRCP, Thomas M MacDonald, ProfFRCP, Steve Morant, PhD, David J Webb, ProfFMedSci, Peter Sever, ProfFRCP, Gordon McInnes, ProfFRCP, Ian Ford, ProfPhD, J Kennedy Cruickshank, ProfFRCP, Mark J Caulfield, ProfFMedSci, Jackie Salsbury, ProfRGN, Isla Mackenzie, FRCP, Sandosh Padmanabhan, FRCP, Morris J Brown, ProfFMedSci

The Lancet

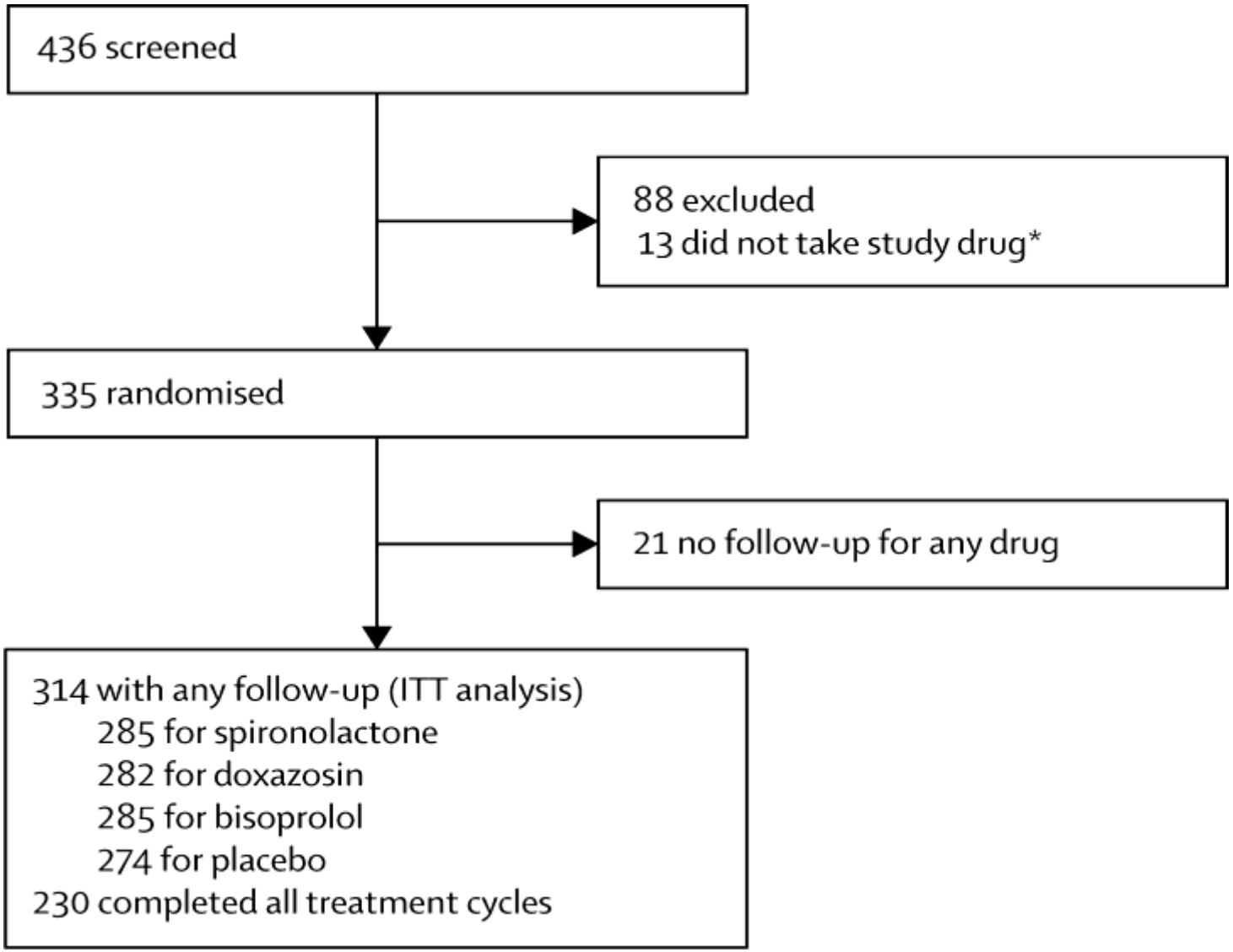
DOI: 10.1016/S0140-6736(15)00257-3

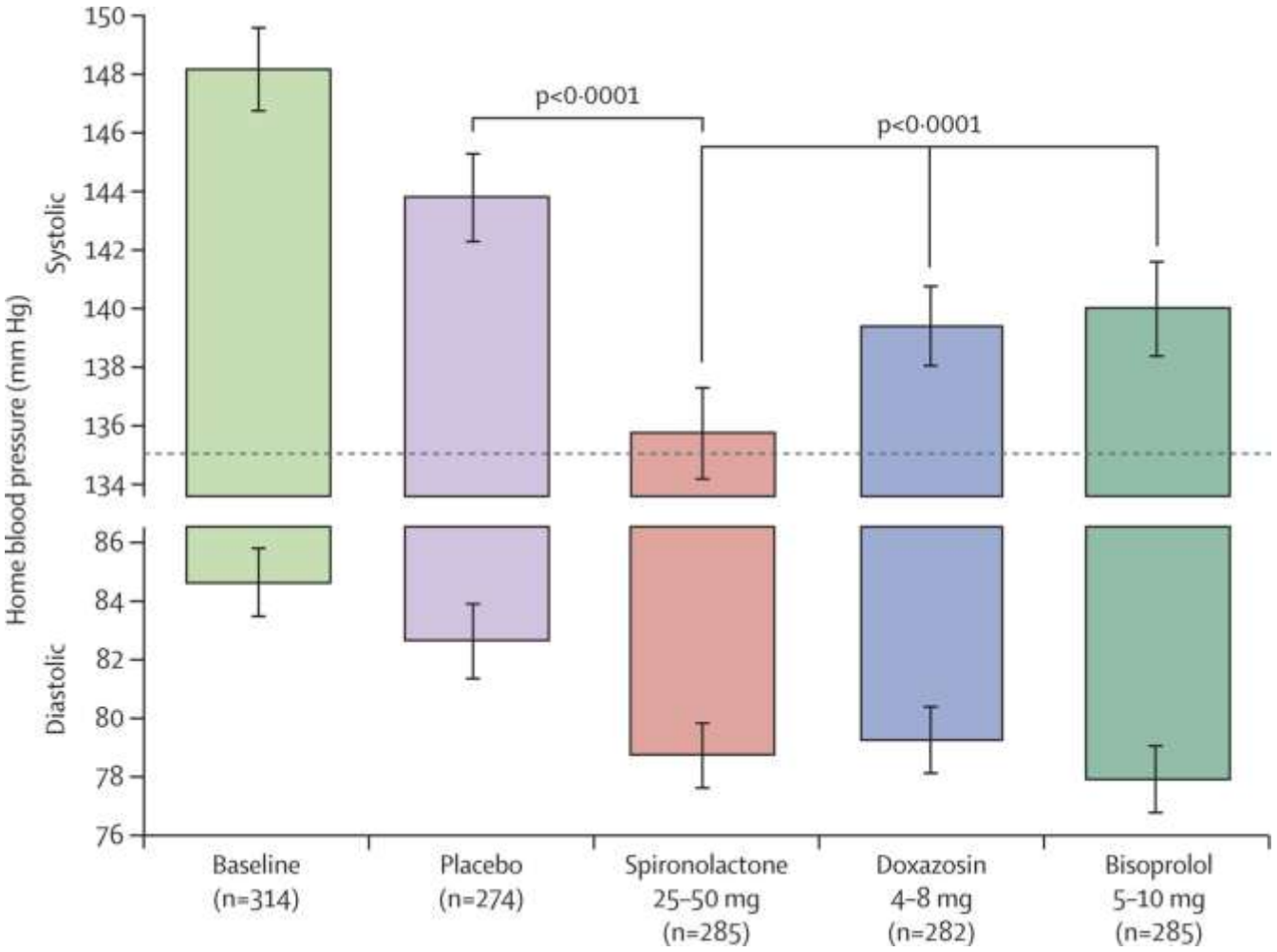
PATHWAY 2 study design and flow chart.



Bryan Williams et al. BMJ Open 2015;5:e008951

BMJ Open





Home systolic blood pressure at final visit of each cycle Home systolic blood pressure at final visit of each cycle

	Blood pressure (mm Hg)	Change from baseline (mm Hg)
Mean		
Spironolactone	133·5 (132·3 to 134·8)	-14·4 (-15·6 to -13·1)
Doxazosin	138·8 (137·6 to 140·1)	-9·1 (-10·3 to -7·8)
Bisoprolol	139·5 (138·2 to 140·8)	-8·4 (-9·7 to -7·1)
Placebo	143·7 (142·5 to 145·0)	-4·2 (-5·4 to -2·9)
Mean differences		
Spironolactone vs placebo	-10·2 (-11·7 to -8·74)	p<0·0001
Spironolactone vs mean bisoprolol and doxazosin	-5·64 (-6·91 to -4·36)	p<0·0001
Spironactone vs doxazosin	-5·30 (-6·77 to -3·83)	p<0·0001
Spironolactone vs bisoprolol	-5·98 (-7·45 to -4·51)	p<0·0001

Home systolic blood pressure dose response (higher *vs* lower dose)

	Blood pressure (mm Hg)	p value
Spironolactone	−3·86 (−5·28 to −2·45)	<0·0001
Doxazosin	−0·88 (−2·32 to 0·56)	0·23
Bisoprolol	−1·49 (−2·94 to −0·04)	0·04
Placebo	−0·68 (−2·10 to 0·75)	0·35

Conclusions

Our finding, that spironolactone was clearly the most effective treatment for resistant hypertension, should influence future treatment guidelines and clinical practice globally. The finding could indeed stimulate an early redefinition of resistant hypertension to include a trial of spironolactone before the label is applied. A longer-term question is whether the antecedent to resistant hypertension is under treatment or wrong treatment, with the resistance to conventional drugs marking a subpopulation in whom spironolactone should be used at an earlier stage.