HOSPITAL UNIVERSITARIO DE SALAMANCA

CVT- 27/11/2014

Lo más relevante del 2014:

Cardiólogo clínico

Francisco Martín Herrero

Complejo Asistencial

Universitario Salamanca

HOSPITAL UNIVERSITARIO DE SALAMANCA

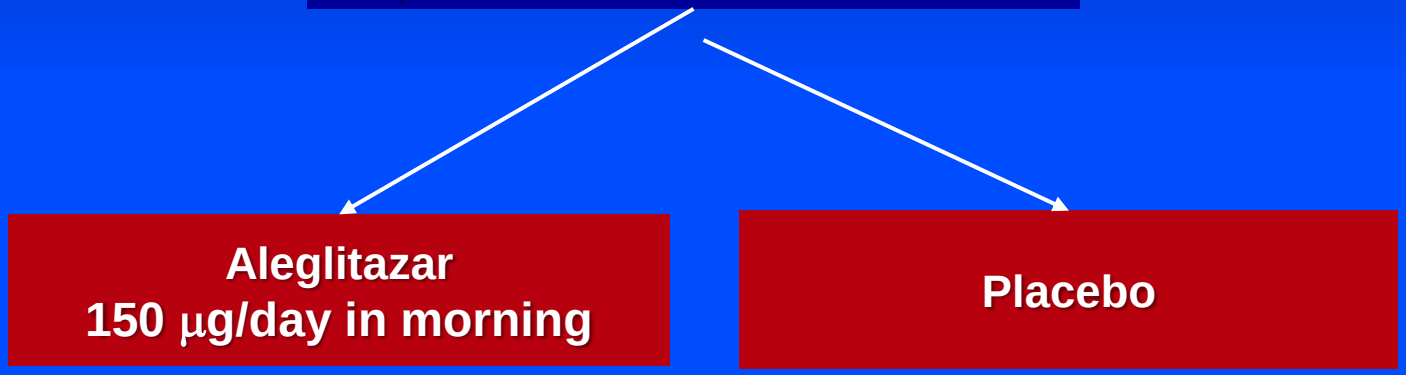
ACC.14

63rd Annual Scientific Session & Expo

Trial Design

Type 2 DM and recent Acute Coronary Syndrome
(STEMI, NSTEMI or UA)

N ~ 7000 Patients Randomized
Double blind, 1:1 Ratio
Up to 12 weeks after index event

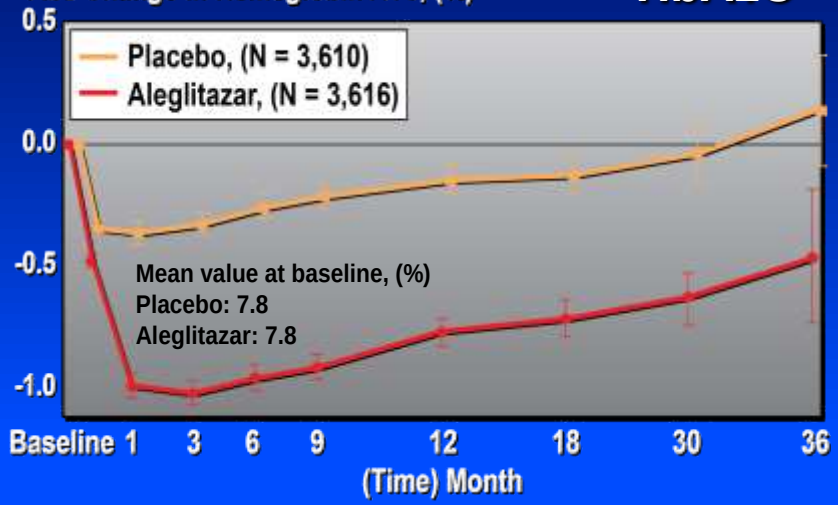


Study visits: 1, 3, 6, 9, 12 mos, then alternative visits and phone q3 mos

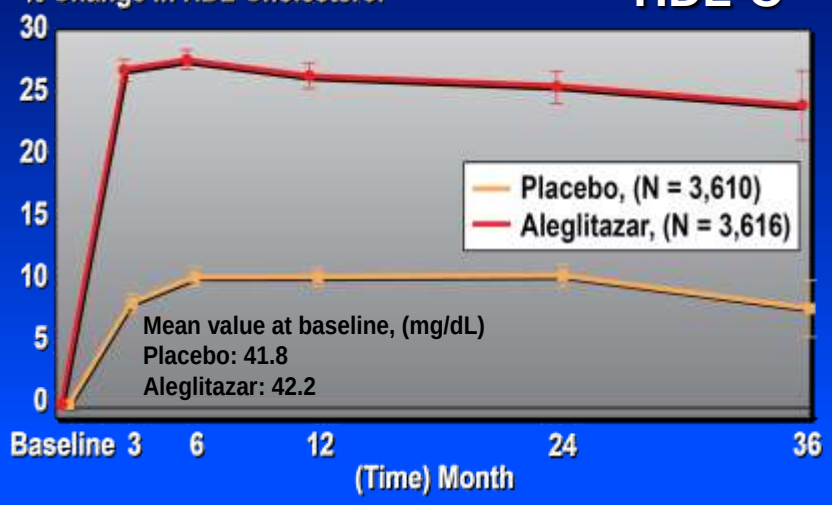
Event Driven – 950 positively-adjudicated 1º Endpoint events
Anticipated ~2.5 years follow-up

Glycemic Control and Lipids

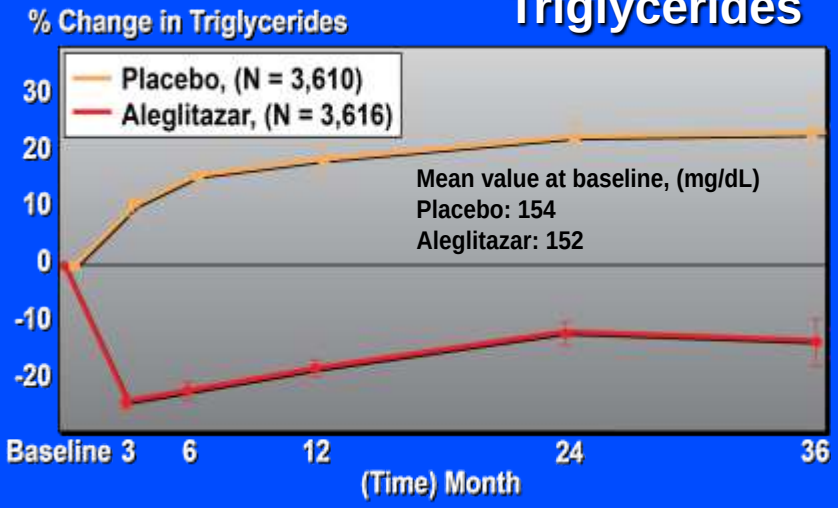
HbA1C



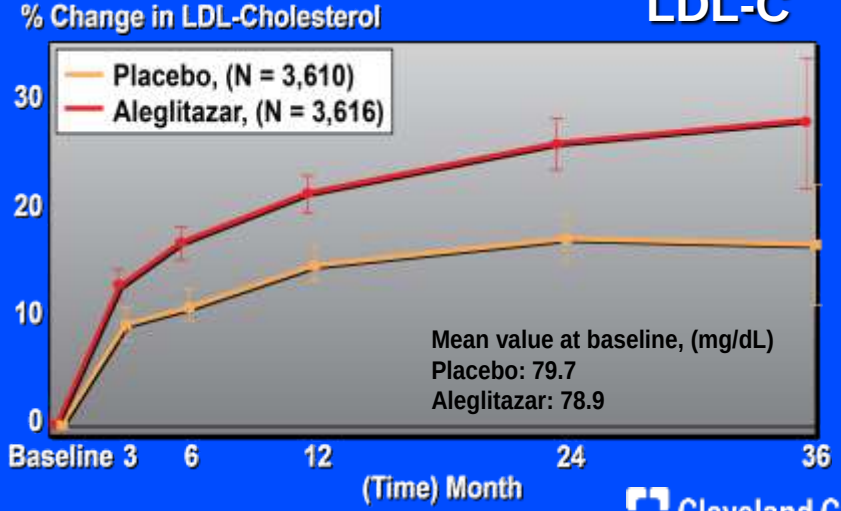
HDL-C



Triglycerides



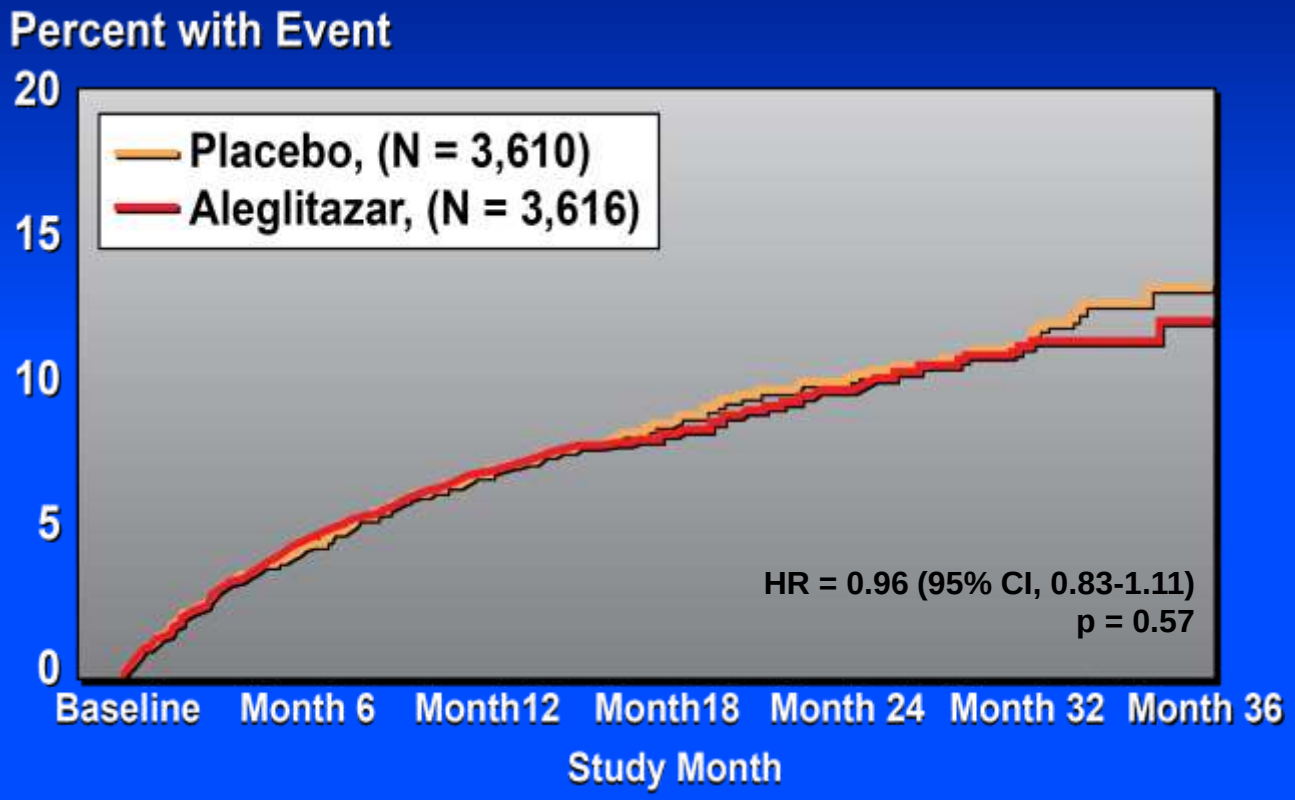
LDL-C



Cleveland Clinic
AML

Primary Efficacy Endpoint

Cardiovascular Death, Non-Fatal MI, Non-Fatal Stroke

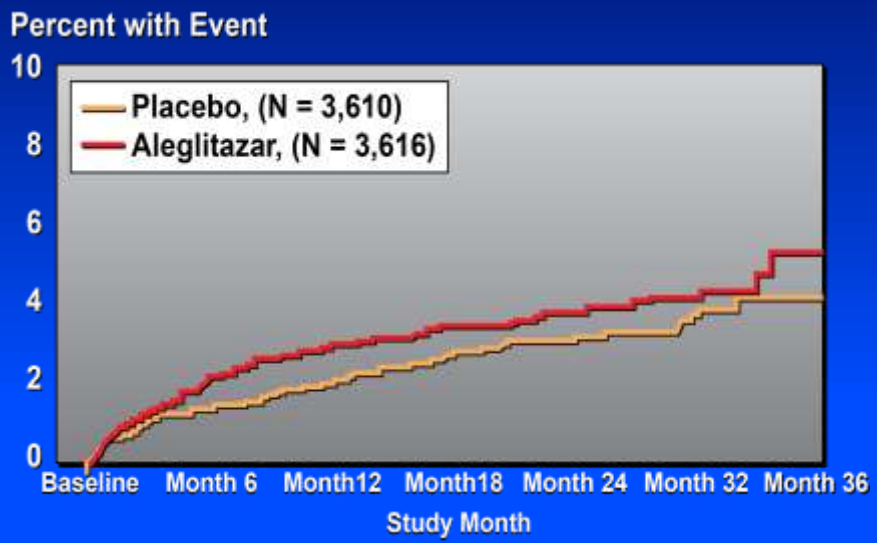


No. at risk:							
Placebo	3610	3394	3252	2720	1706	773	118
Aleglitazar	3616	3387	3249	2731	1688	780	101

Cleveland Clinic
AML

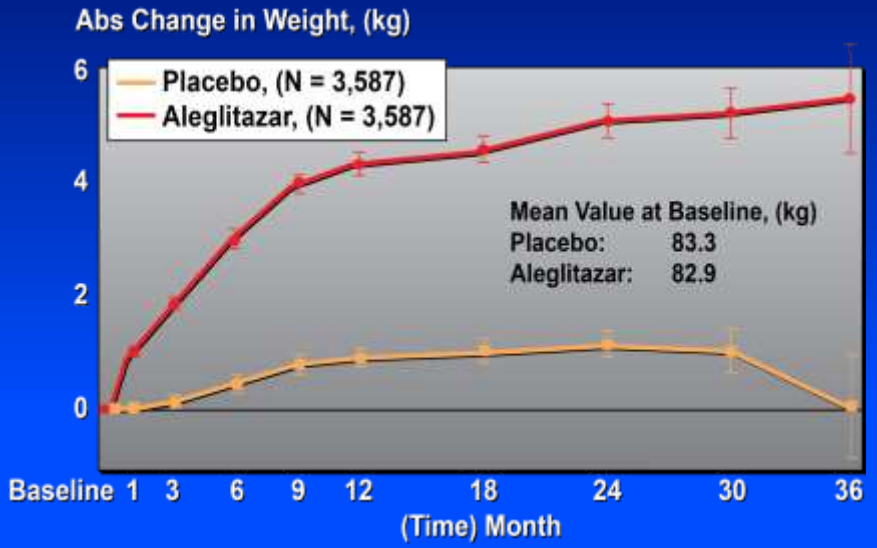
Heart Failure/Fluid Retention

Hospitalization for HF



HR = 1.22 (95% CI, 0.94-1.59)
p = 0.14

Body Weight



4.6 kg vs. 0.9 kg, P <0.001

Heart Failure Serious Adverse Event:

Aleglitazar 4.7% vs Placebo 3.8%, HR 1.24; 95% CI 0.99 to 1.66, P = 0.06

Peripheral Edema:

Aleglitazar 14.0% vs Placebo 6.6%, P <0.001

Cleveland Clinic
AML

Undetectable High Sensitivity Cardiac Troponin T Level in the Emergency Department and Risk of Myocardial Infarction

Nadia Bandstein, MD; Rickard Ljung, MD, PhD; Magnus Johansson, MD, PhD; Martin Holzmann, MD, PhD.

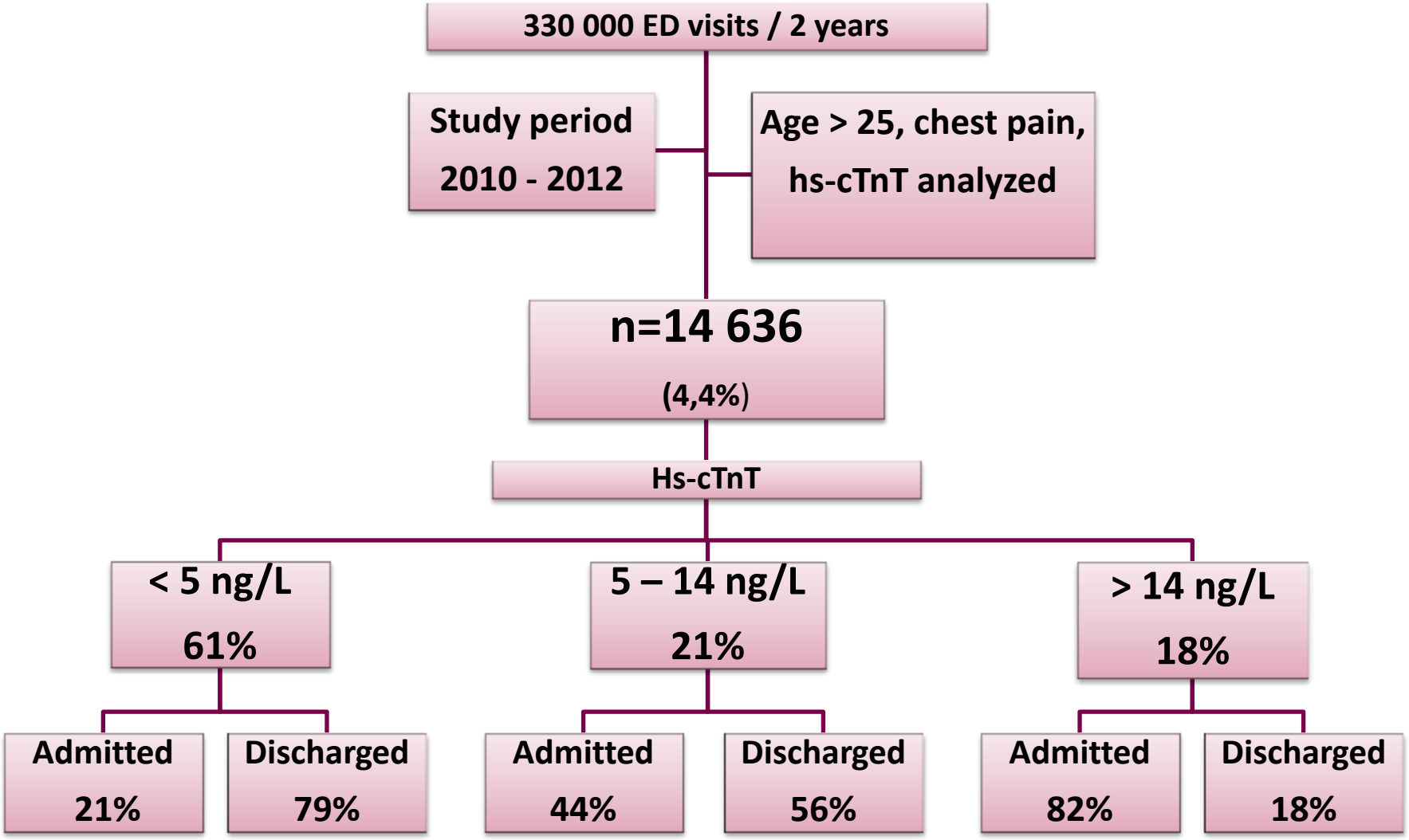
Department of Emergency Medicine
Karolinska University Hospital and Karolinska Institute
Stockholm, Sweden

Late Breaking Clinical Trial, ACC.14, Washington

Hypothesis

- All patients with chest pain, who have an undetectable high-sensitivity cardiac troponin T (< 5 ng/l), and an ECG without signs of ischemia, may be discharged directly from the emergency department (ED), since their risk of MI within 30 days is minimal.

Study population



Risk of Myocardial Infarction

	High-Sensitivity Cardiac Troponin T level (ng/L)		
	<5	**5-14**	**>14**
Myocardial infarction			
30 days			
Number of events	**15**	97	676
Negative pred. val.	**99,8 (99,7-99,9)**	96,9 (96,3-97,5)	73,8 (72,1-75,5)
365 days			
Number of events	54	134	753
Negative pred. val.	99,4 (99,2-99,5)	95,7 (95,0-96,5)	70,8 (69,0-72,6)

HOSPITAL UNIVERSITARIO DE SALAMANCA

ESC CONGRESS

BARCELONA 2014

30 Aug - 3 Sept

EUROPEAN SOCIETY OF CARDIOLOGY®

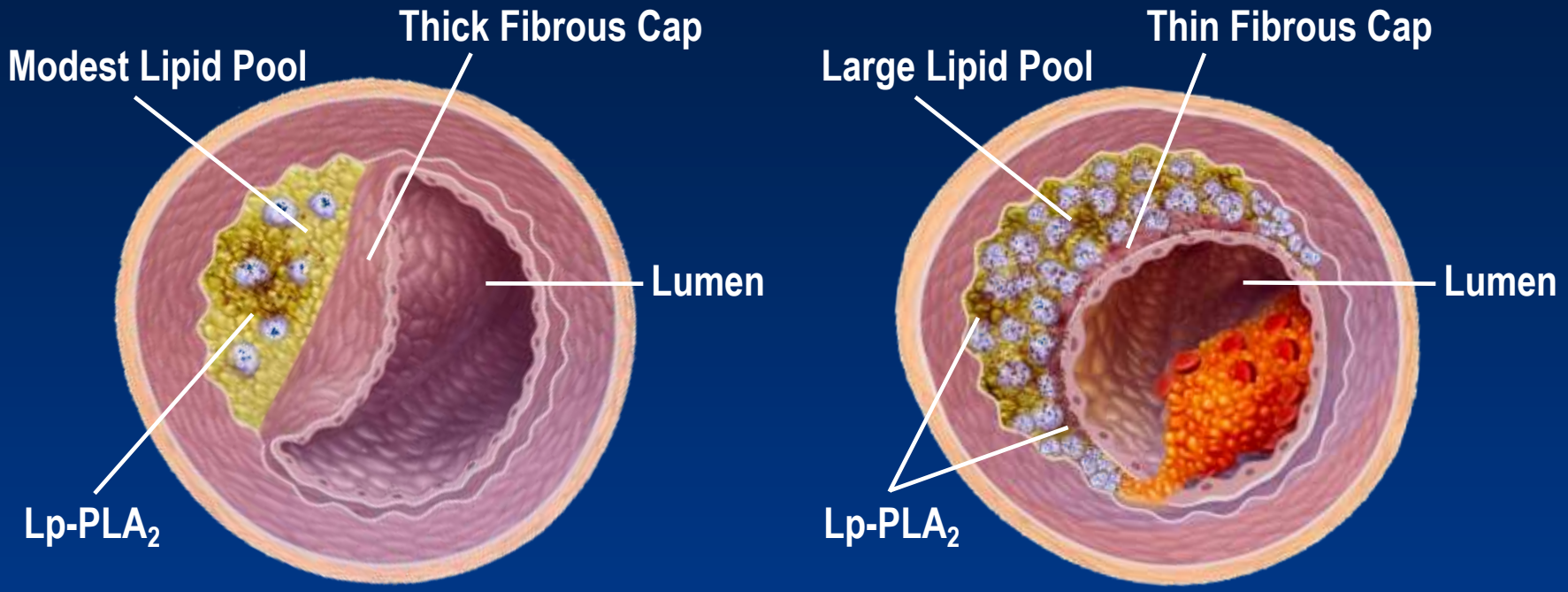
The Stabilization Of pLaques usIng Darapladib (SOLID)-TIMI 52 trial: Primary Results

Michelle L. O'Donoghue MD MPH, on behalf of the SOLID-TIMI 52 investigators

European Society of Cardiology Congress
Barcelona, Spain
Sunday August 31, 2014

BRIGHAM AND WOMEN'S HOSPITAL
| Heart & Vascular Center |

Characteristics of Stable versus Ruptured Plaques



Stable Plaque	Ruptured Plaque
✓ Low Lp-PLA_2 content (dark staining)	✓ High Lp-PLA_2 content (dark staining)
✓ May have significant stenosis	✓ May have minimal stenosis
✓ Thick fibrous cap / high collagen content	✓ Thin fibrous cap / low collagen content
✓ Modest lipid pool	✓ Large lipid pool
✓ Few inflammatory cells	✓ Many inflammatory cells

Corson et al. Am J Card 2008;101(Suppl):41F-50F

Darapladib Phase III Clinical Program

High risk* patients with chronic CHD

Randomization to Darapladib or Placebo

n= 15,898
(3.7 year median f/u)

High risk* patients with ACS (STEMI, NSTEMI, UA)

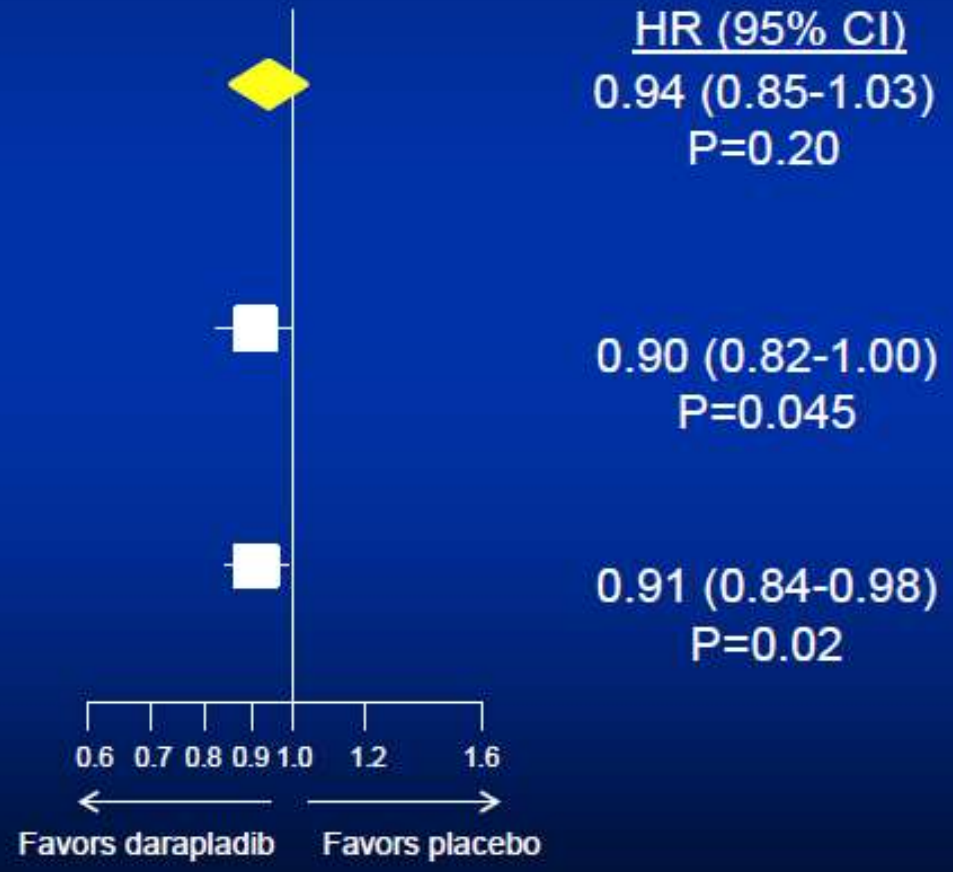
Randomization to Darapladib or Placebo within 30 days of index event

n= 13,026
(2.5 year median f/u)

* High-risk criteria (≥1 of the following): age >60 years, diabetes mellitus, (eGFR 30-60 ml/min/1.73 m^2), polyvascular disease, HDL <40 mg/dl (STABILITY only), tobacco use (STABILITY only), or prior MI (SOLID-TIMI 52 only)

STABILITY Trial

15,828 patients with stable CHD randomized to darapladib 160mg QD vs placebo



Primary Endpoint

CV death, MI or stroke

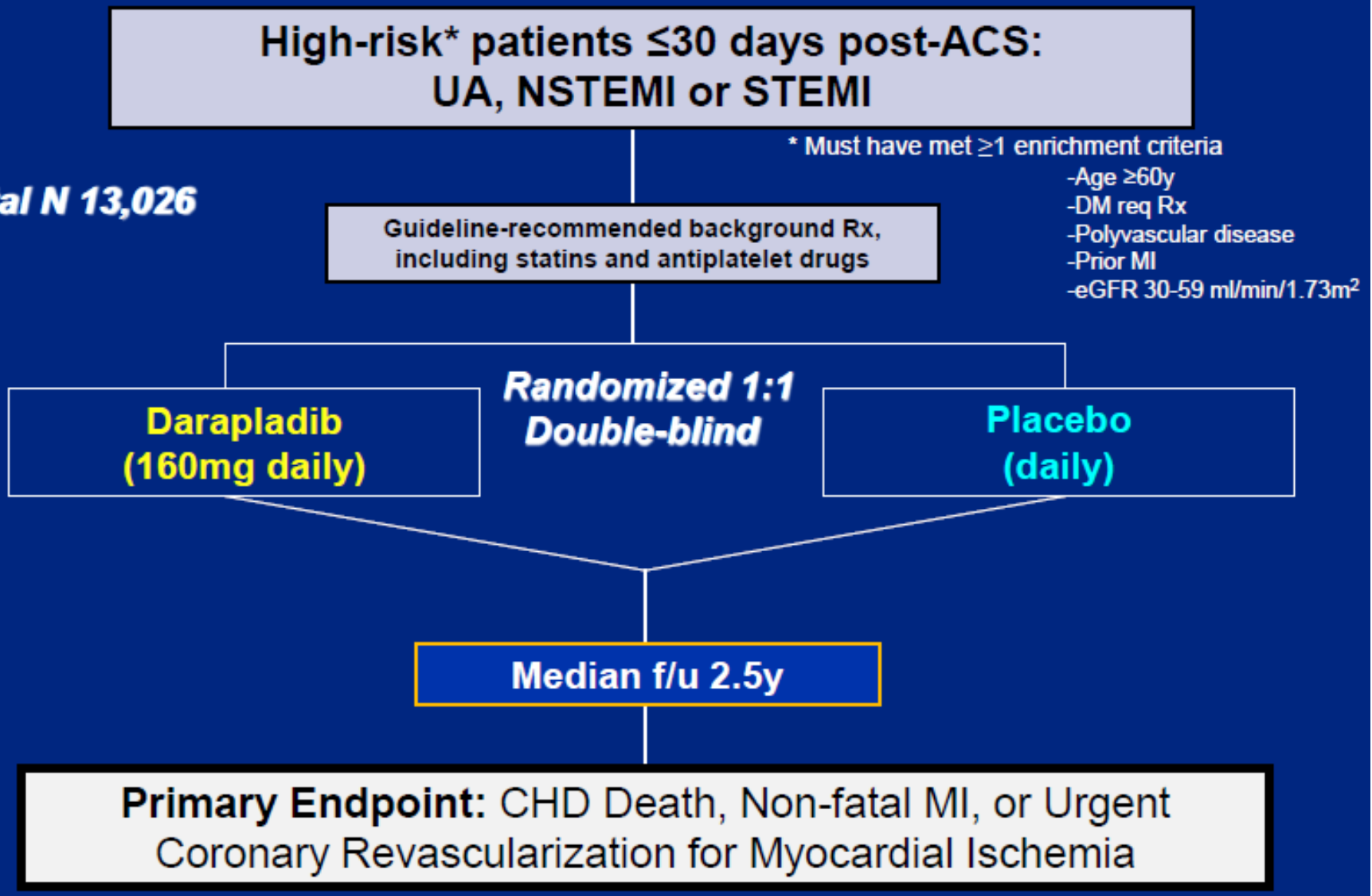
Selected Secondary Endpoints

Major Coronary Events:
(CHD death, MI or urgent coronary revascularization for myocardial ischemia)

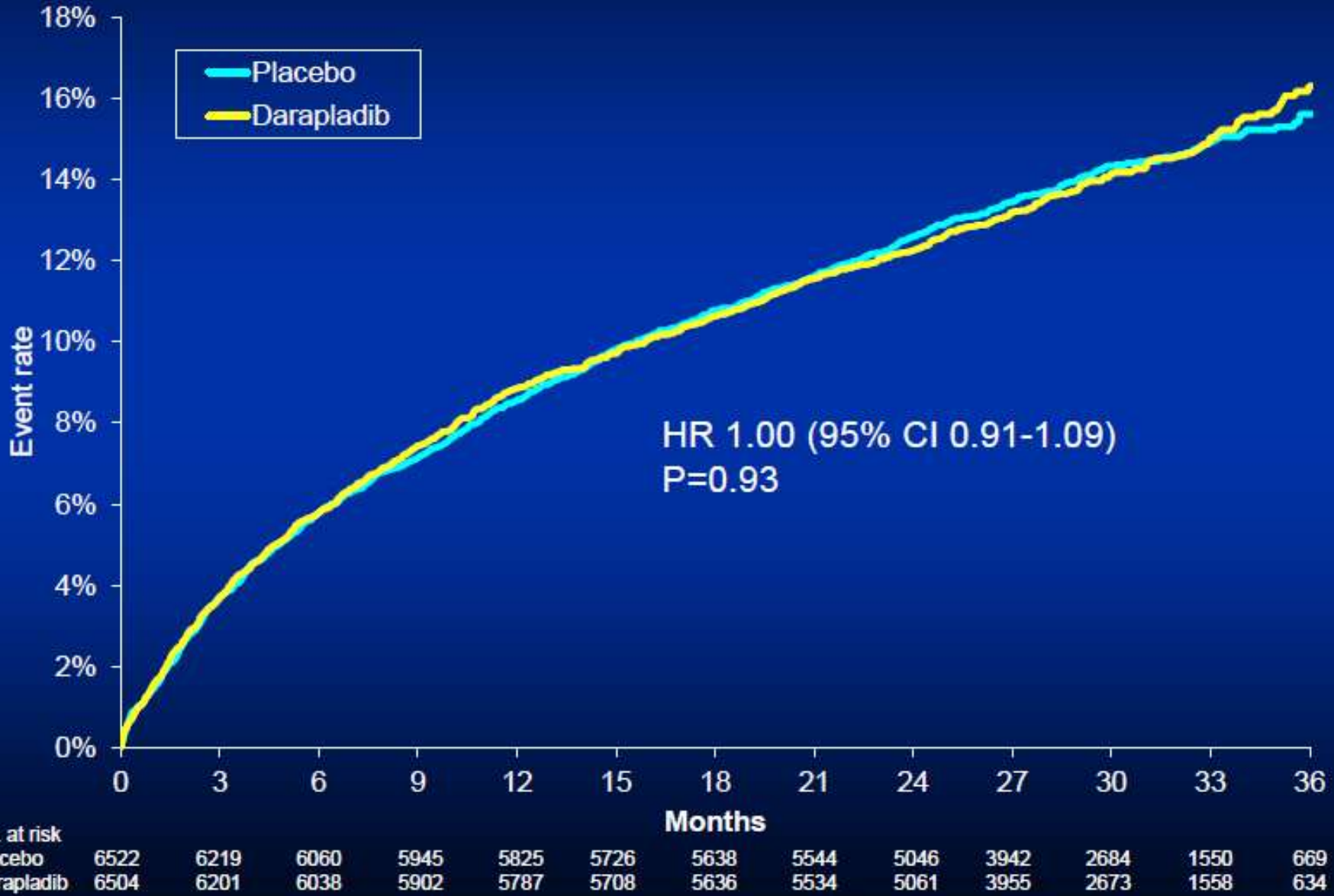
Total Coronary Events
(CHD death, MI, hospitalization for UA or any coronary revascularization)

White et al., *N Engl J Med* 2014; 370:1702-11.

SOLID-TIMI 52 Study Design



Primary Endpoint: CHD death, MI or urgent coronary revascularization



No. at risk													
Placebo	6522	6219	6060	5945	5825	5726	5638	5544	5046	3942	2684	1550	669
Darapladib	6504	6201	6038	5902	5787	5708	5636	5534	5061	3955	2673	1558	634

ATLANTIC

Administration of **T**icagrelor in the cath **L**ab or in the **A**mbulance for **N**ew S**T** elevation myocardial **I**nfarction to open the **C**oronary artery

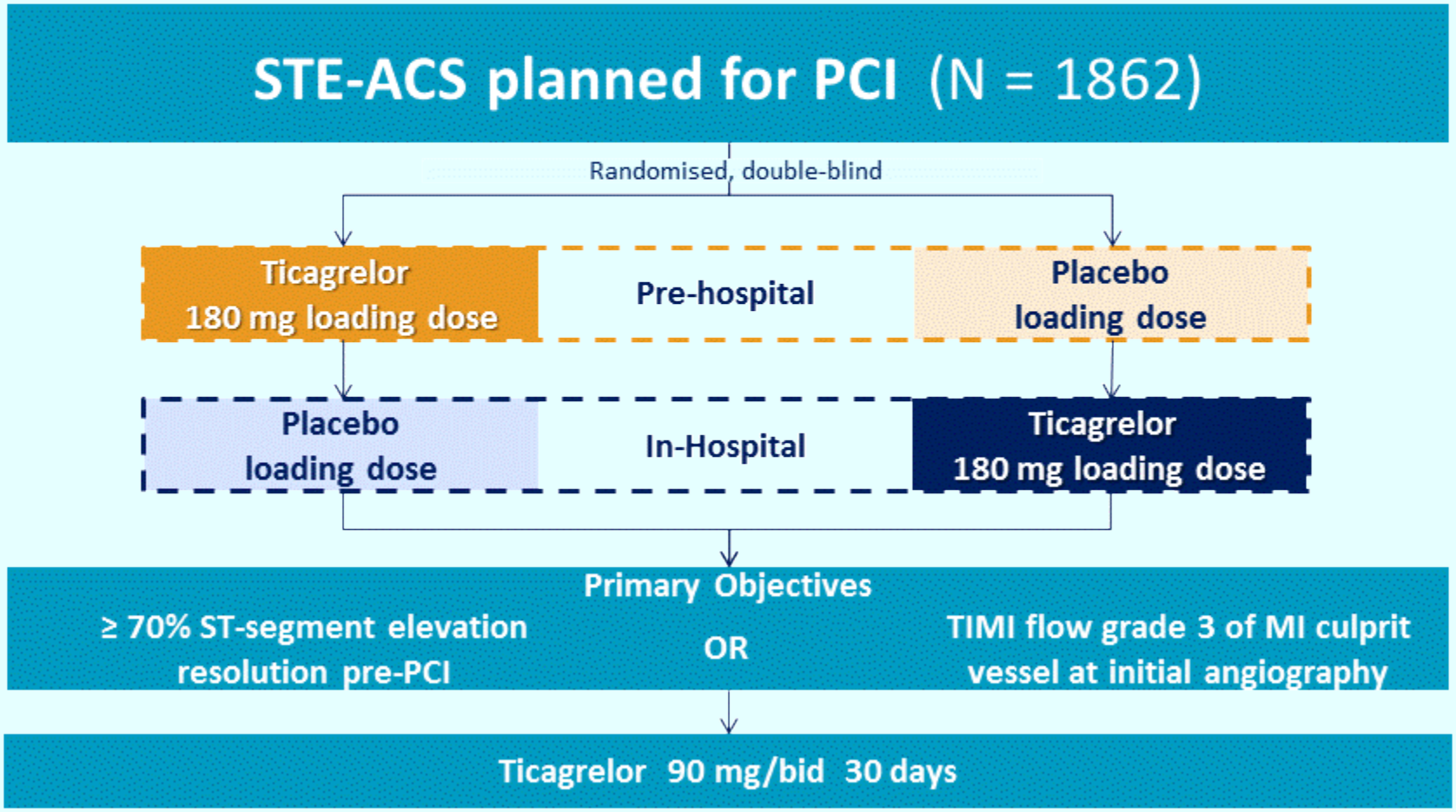
G. Montalescot, A.W. van't Hof, F. Lapostolle, J Silvain, J.F. Lassen, L. Bolognese, W.J. Cantor, A. Cequier, M. Chettibi, S.G. Goodman, C.J. Hammett, K. Huber, M. Janzon, B. Merkely, R.F. Storey, U. Zeymer, O. Stibbe, P. Ecollan, W.M.J.M. Heutz, E. Swahn, J.P. Collet, F.F. Willems, C. Baradat, M. Licour, A. Tsatsaris, E. Vicaut, C.W. Hamm, for the ATLANTIC investigators

G. Montalescot, COI are available at www.action-coeur.org

Study population and design

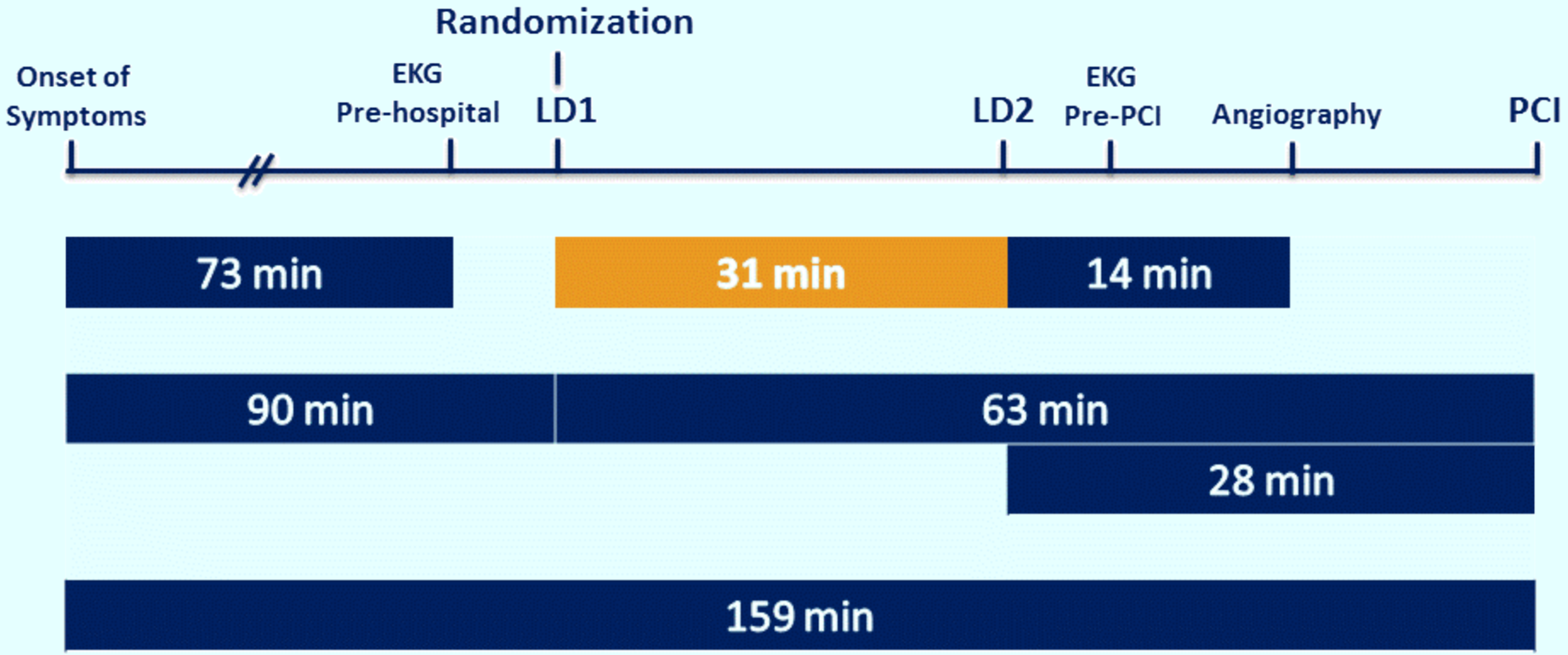
Atlantic Population

- Documented evidence of **STEMI**
- Planned for **angioplasty (PCI)**
- **onset of ischaemic symptoms within 6 h**
- **initially managed by ambulance physician/personnel**; also concerning patients not pre-treated for STEMI in **emergency rooms of non-PCI hospitals**



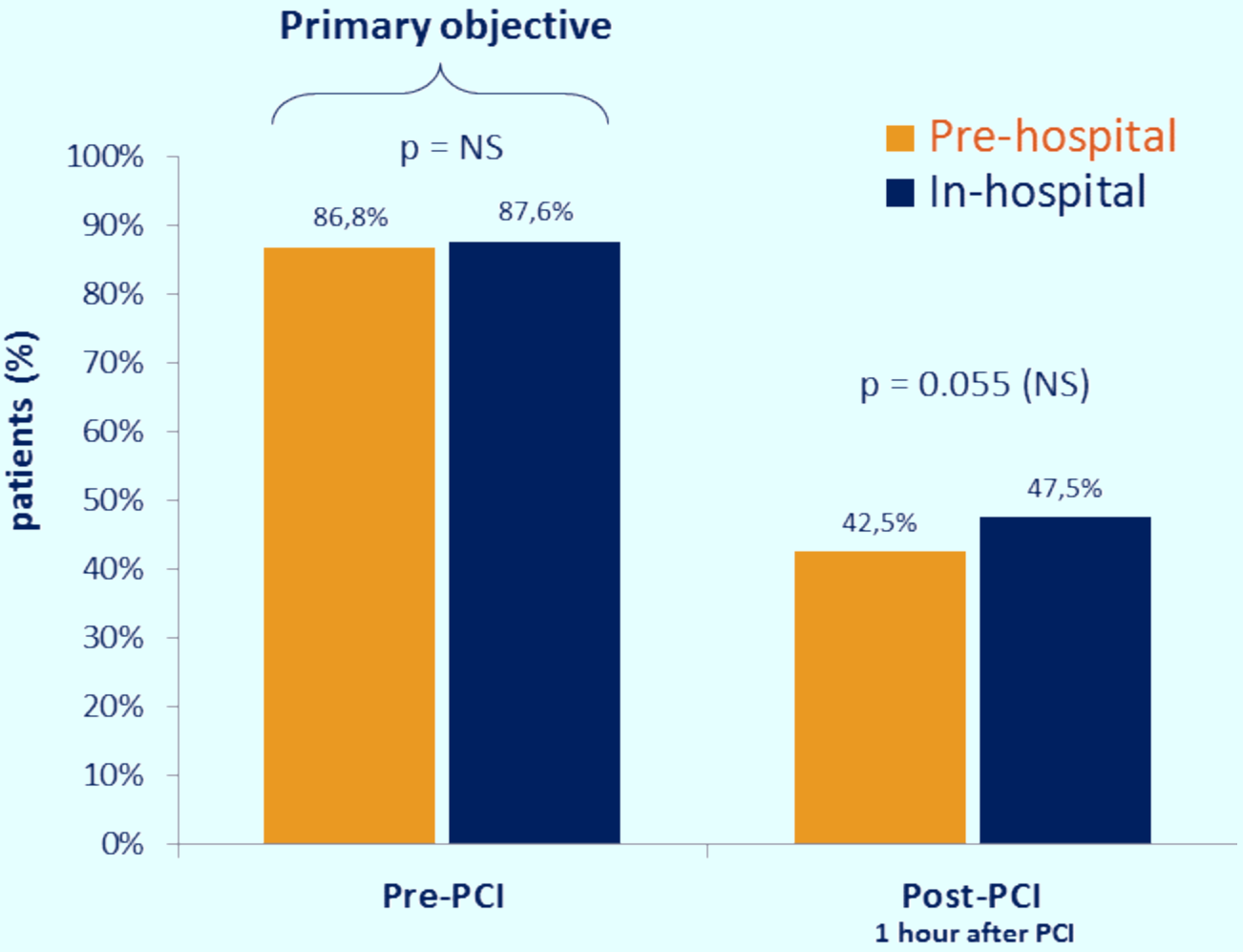
Montalescot G et al. *Am Heart J.* 2013;165:515–522.

Median times to pre- and in-hospital steps



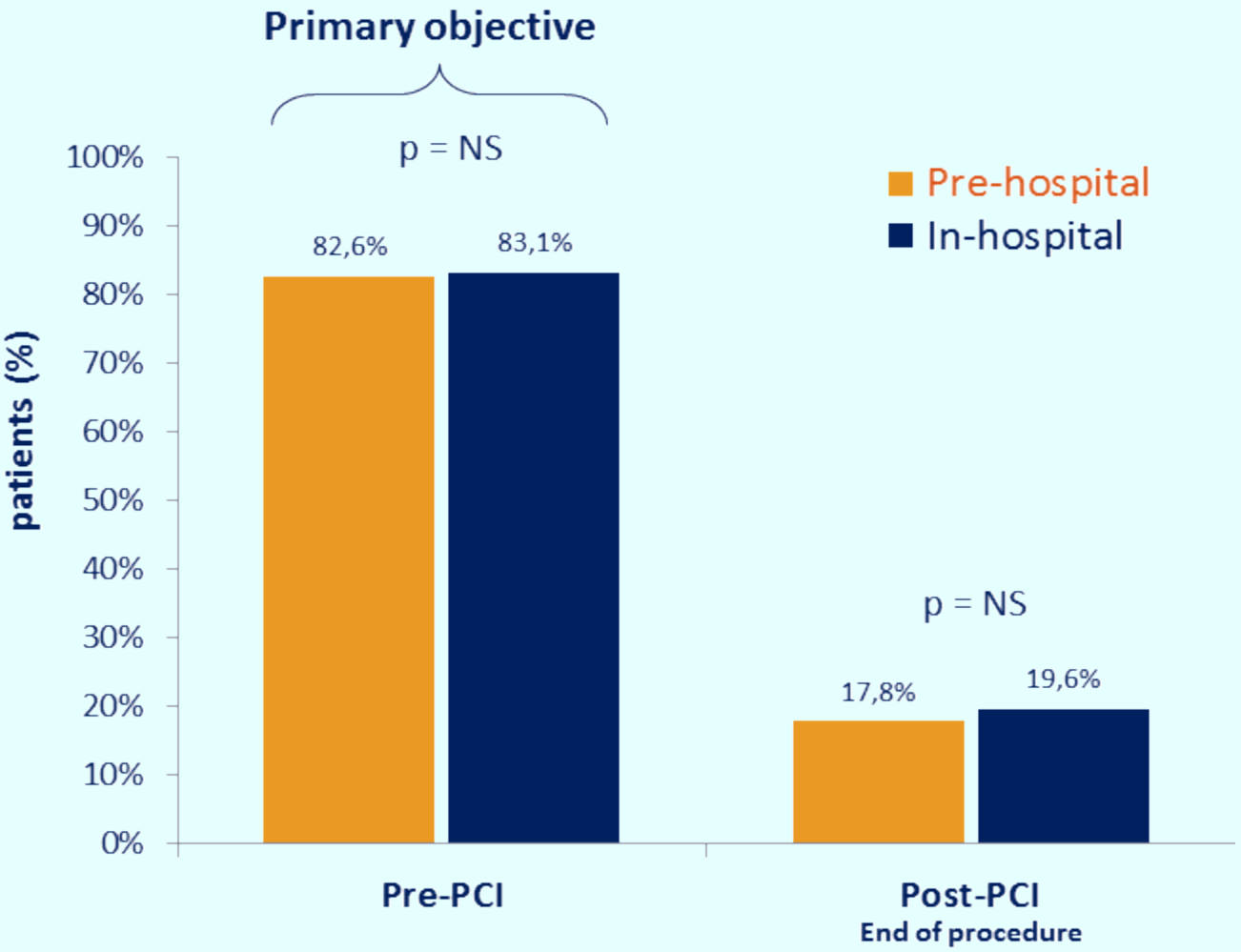
1st Co-primary endpoint

No ST-segment resolution (≥70%)

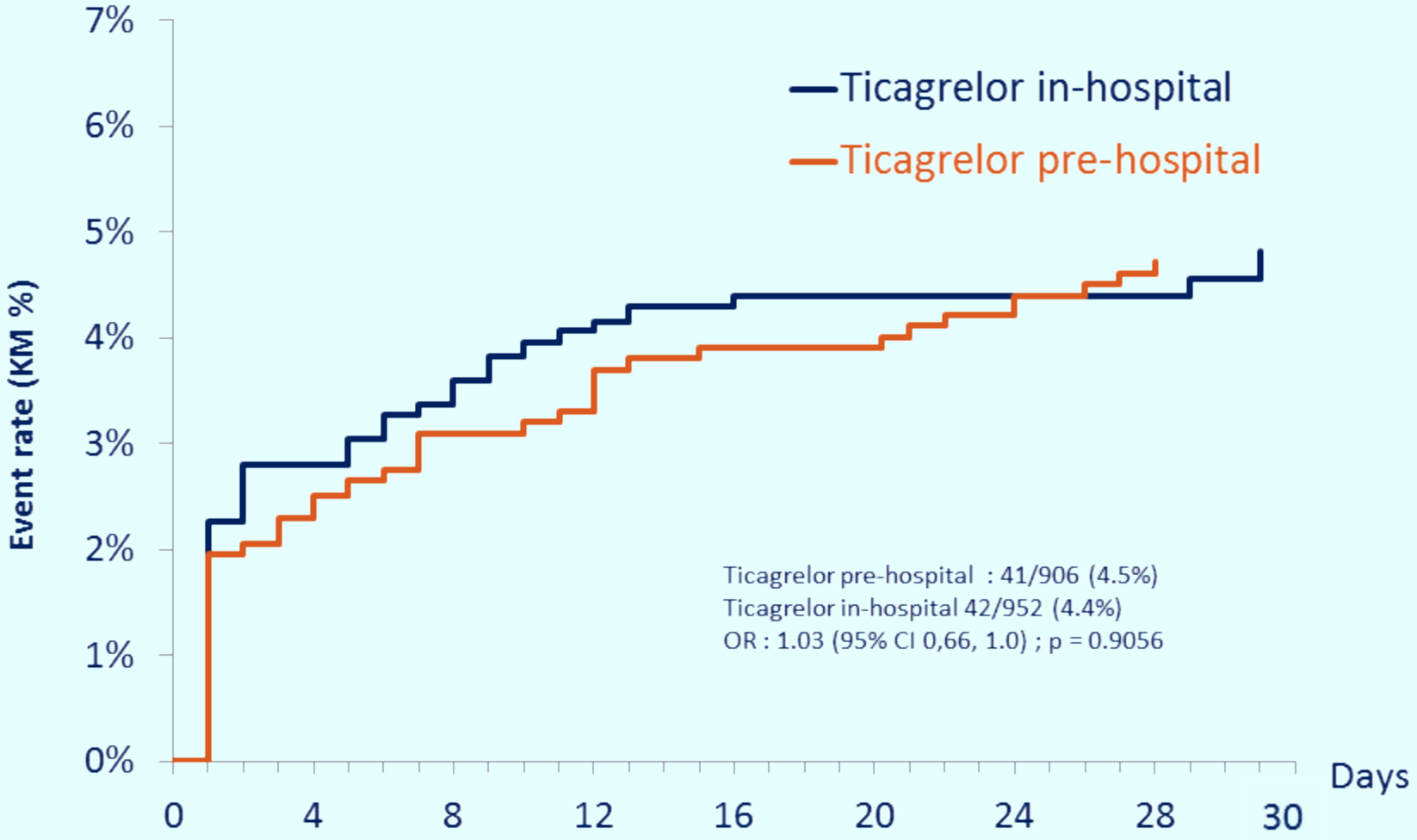


2nd Co-primary endpoint

No TIMI 3 flow in infarct-related artery

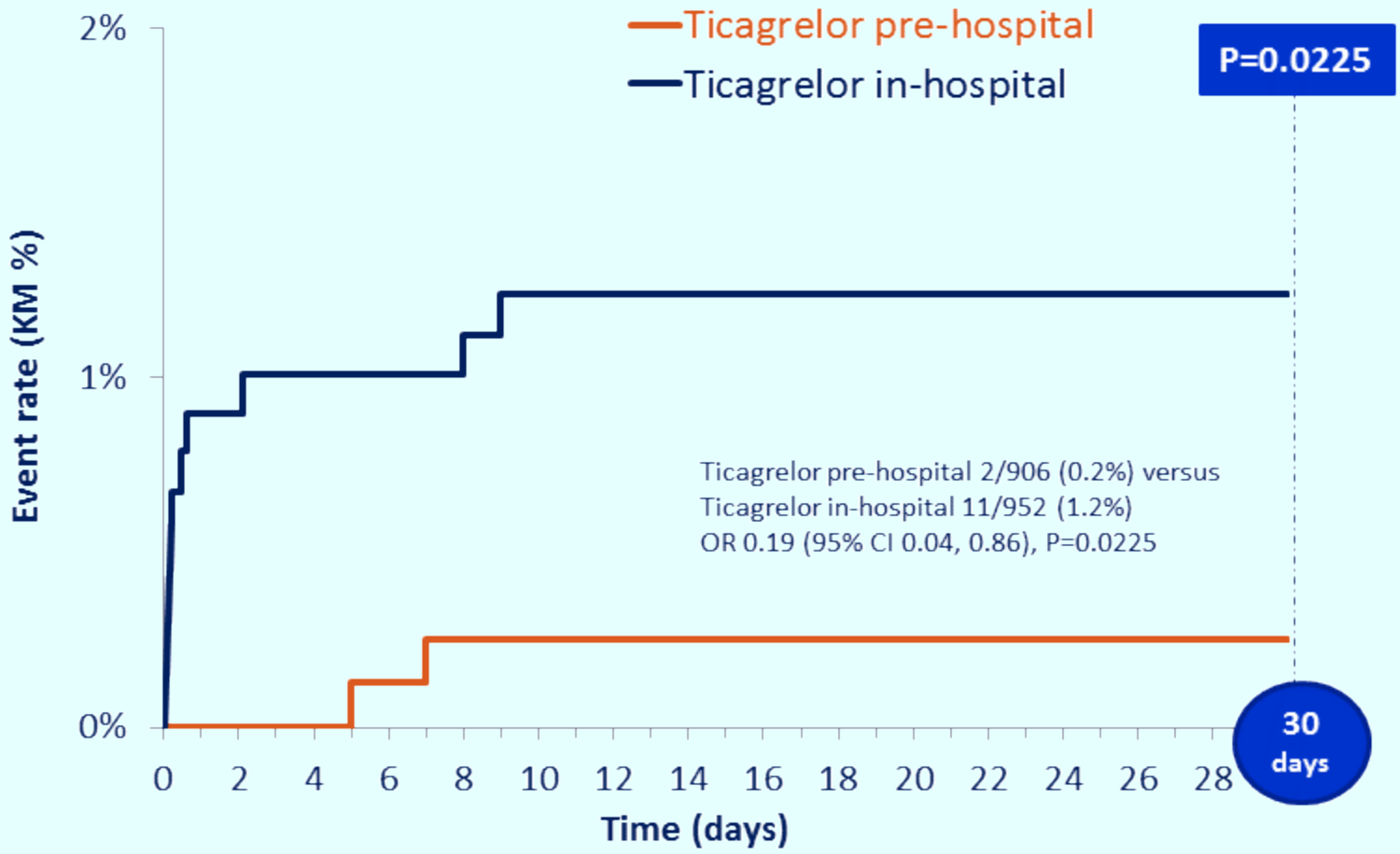


Major adverse CV events up to 30 days

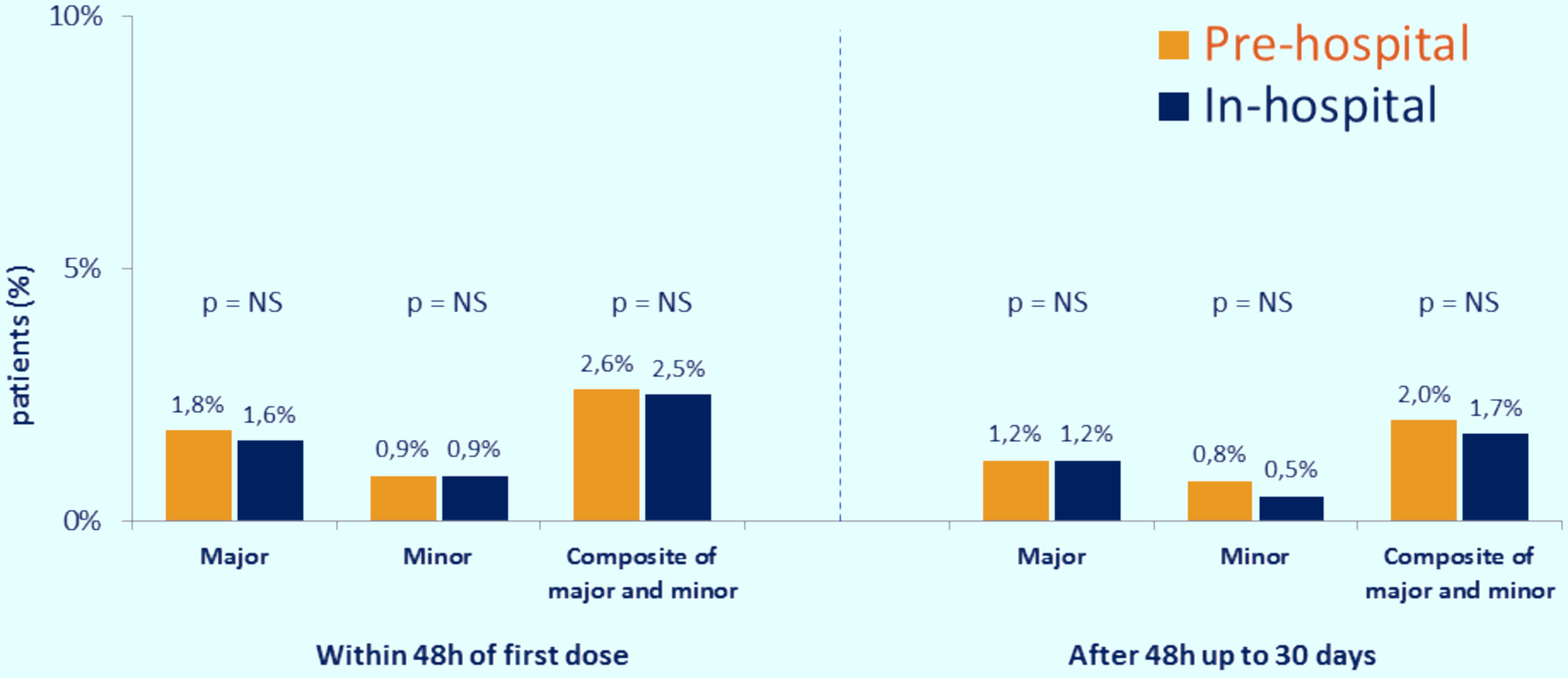


MACE: death, MI, stent thrombosis, stroke or urgent revascularization

Definite stent thrombosis up to 30 days



Non-CABG-related bleeding events
(PLATO definitions) - Safety population



HOSPITAL UNIVERSITARIO DE SALAMANCA

American Heart Association®

SCIENTIFIC SESSIONS 2014

AVOID Study

Air Versus Oxygen In ST-elevation MyocarDial Infarction

Dr Dion Stub MBBS PhD FRACP
Baker IDI Heart & Diabetes Institute, Melbourne Australia
St Paul's Hospital Vancouver, Canada

On behalf of Karen Smith, Stephen Bernard, Ziad Nehme, Michael Stephenson, Janet E. Bray, Peter Cameron, Bill Barger, Andris H. Ellims, Andrew J. Taylor, Ian T. Meredith, David M. Kaye for the AVOID Investigators.

Trial Design

Paramedics Assess Patient
Symptoms of STEMI <12 hours, O_2 Sats ≥ 94%
ST-elevation ≥2 contiguous ECG leads
Intended for primary PCI

Exclusion Criteria
Oxygen saturation <94% on pulse oximeter
Oxygen administration prior to randomization
Altered conscious state
Planned transport to a non-participating hospital

Randomize 1:1

Oxygen
8L/minute via face mask

No Oxygen
Unless O2 falls below 94% than minimum titrated O2 via mask

Pre-Hospital

Physician confirms STEMI

In-Hospital

Primary PCI
Oxygen (8L/min) in Cath Lab

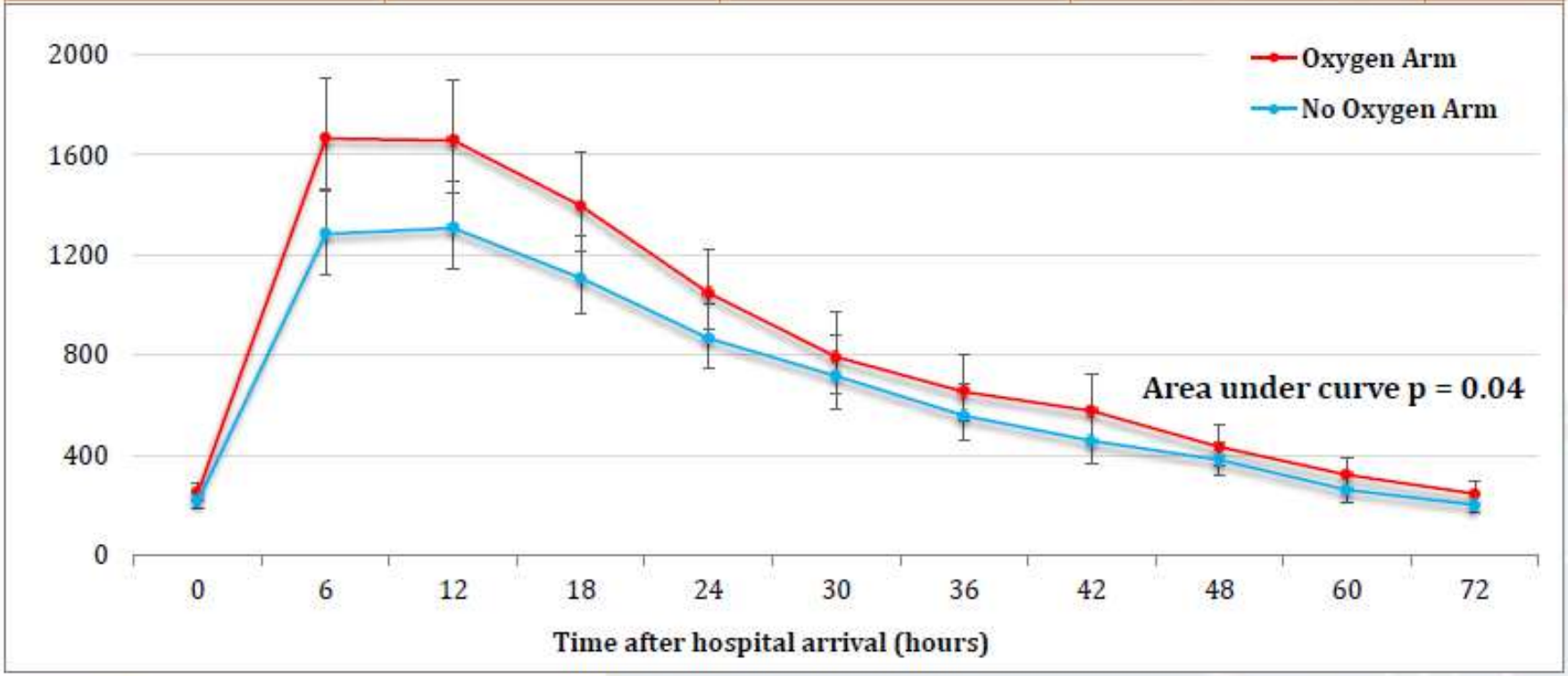
Primary PCI
No Oxygen in Cath Lab

Cardiac Enzymes 72 hours
Cardiac MRI and clinical follow up 6 months

Stub et al. *AHJ* 2012;163;3;339-345
Clinicaltrials.gov NCT01272713

Primary Endpoint Infarct Size on Cardiac Enzymes

Creatine kinase, U/L	Oxygen Arm N=217	No Oxygen Arm N=222	Ratio of means (Oxygen/No Oxygen)	P-value
Geometric Mean Peak (95% CI)	1948 (1721 – 2205)	1543 (1341 – 1776)	1.26 (1.05 – 1.52)	0.01
Median Peak (IQR)	2073 (1065, 3753)	1727 (737, 3598)		0.04



Secondary Endpoint
CMR Infarct Size at 6 months

CMR Infarct Size	Oxygen Arm N=65	No Oxygen Arm N=74	Ratio of means (Oxygen/No Oxygen)	P-value
Median (IQR), grams	20.3 (9.6, 29.6)	13.1 (5.2, 23.6)		0.04
Geometric Mean (95% CI), grams	14.6 (11.3 – 18.8)	10.2 (7.7 – 13.4)	1.43 (0.99 – 2.07)	0.06
Median (IQR) proportion of LV mass	12.6 (6.7, 19.2)	9.0 (4.1, 16.3)		0.08
Geometric Mean(95% CI)proportion of LV mass	10.0 (8.1 – 12.5)	7.3 (5.7 – 9.3)	1.38 (0.99 – 1.92)	0.06

Clinical Endpoints

Values are %	Oxygen Arm N=218	No Oxygen Arm N=223	P-Value
At Hospital Discharge			
Mortality	1.8	4.5	0.11
Recurrent myocardial infarction	5.5	0.9	<0.01
Stroke	1.4	0.4	0.30
Major bleeding	4.1	2.7	0.41
Significant arrhythmia	40.4	31.4	0.05
ECG ST-segment resolution > 70%	62.0	69.6	0.10
At 6 months follow up			
Mortality	3.8	5.9	0.32
Recurrent myocardial infarction	7.6	3.6	0.07
Stroke	2.4	1.4	0.43
Repeat revascularization	11.0	7.2	0.17
MACCE	21.9	15.4	0.08

STEMI Accelerator

Regional Systems of Care Demonstration Project

Final Results of the Regional Systems of Care Demonstration Project: Mission: Lifeline™ *STEMI Accelerator* Study

Matthew W Sherwood, Hussein R Al-Khalidi, James G Jollis, Mayme L Roettig, Peter B Berger, Claire C Corbett, Harold L Dauerman, Kathleen Fox, J Lee Garvey, Timothy D Henry, Ivan C Rokos, B Hadley Wilson, Christopher B. Granger for the Accelerator Project

Duke Clinical Research Institute

American Heart Association. | MISSION: LIFELINE

Intervention Sites

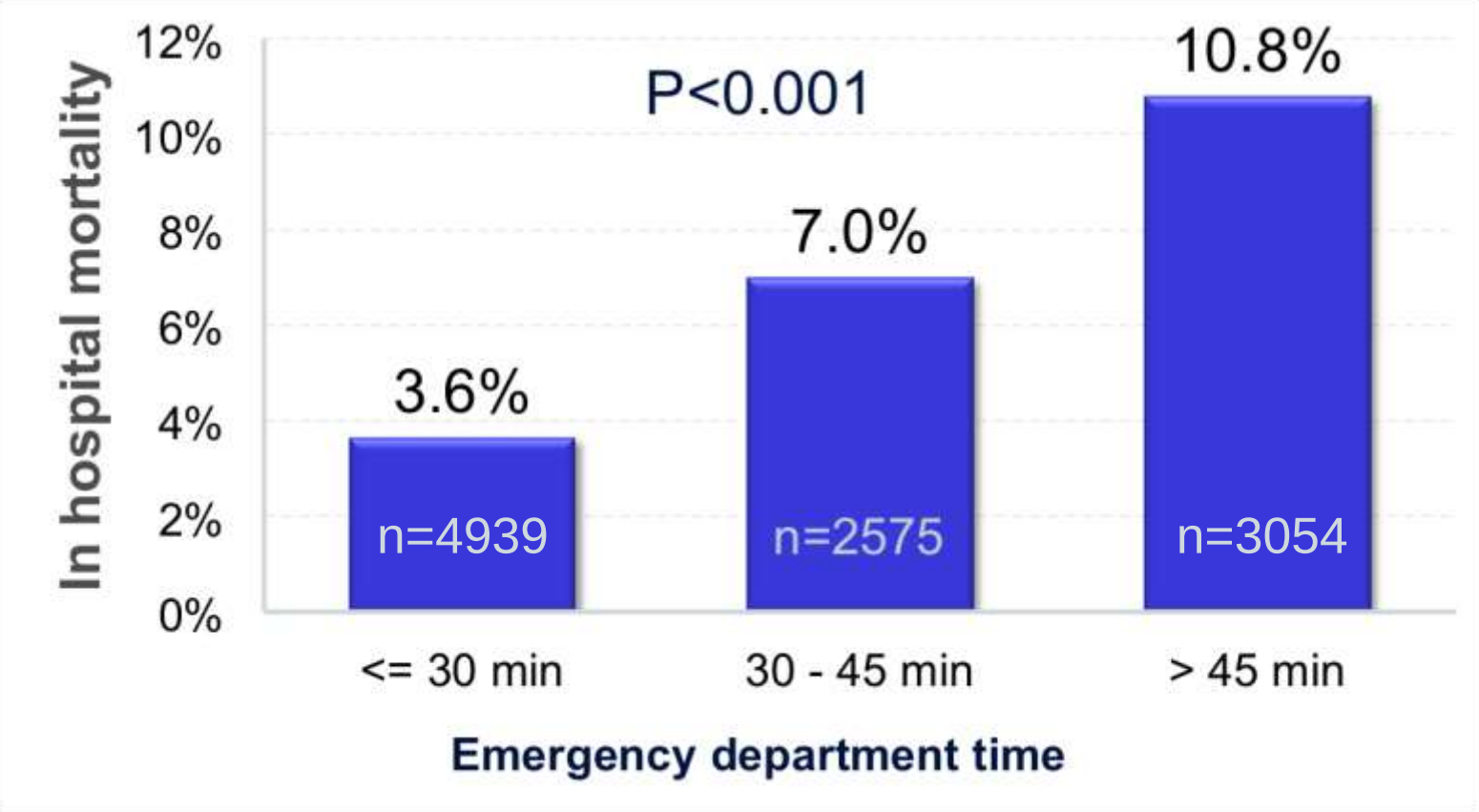
16 regions
484 hospitals
1,253 EMS agencies

Duke Clinical Research Institute

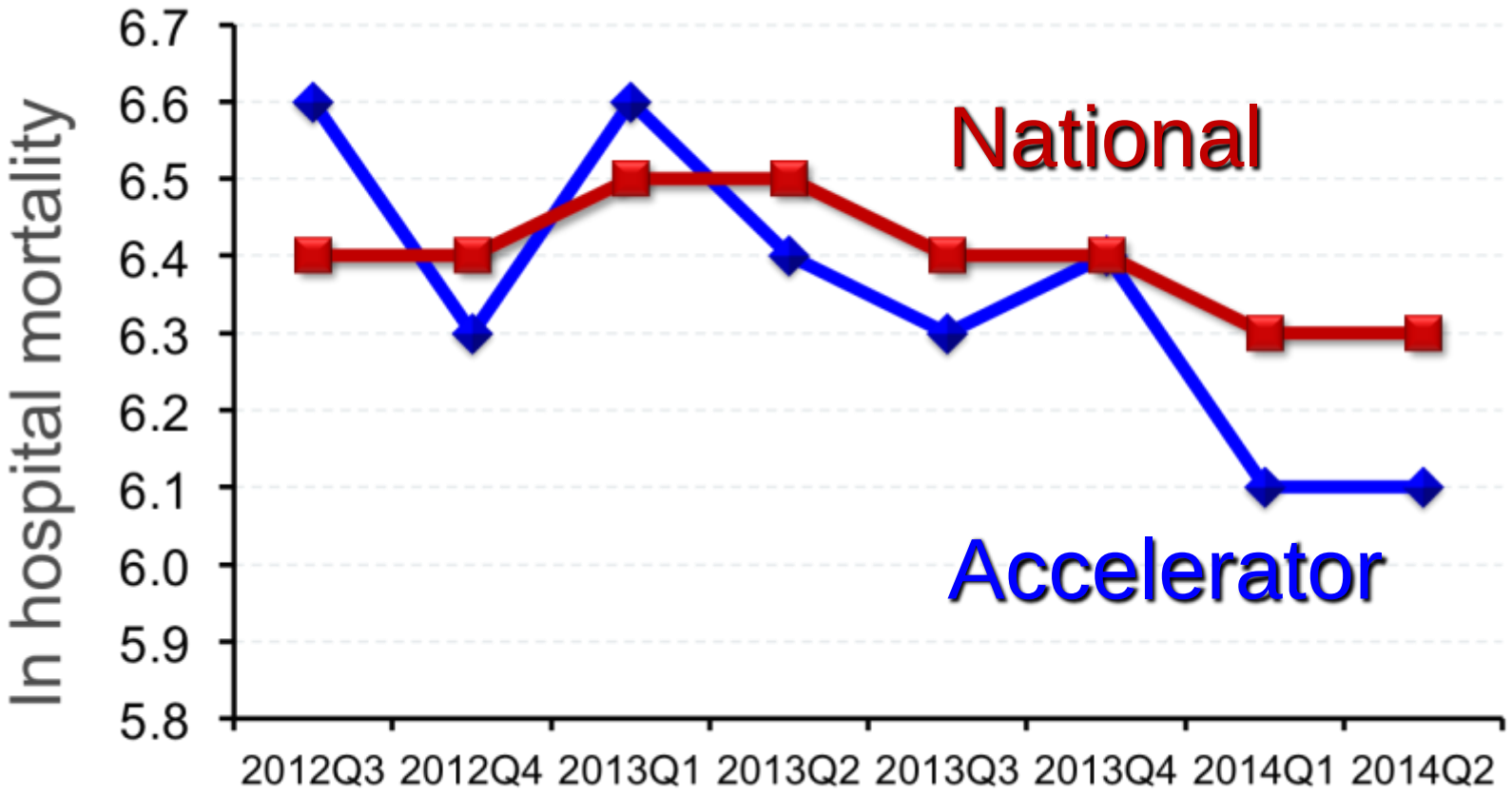
American Heart Association. | MISSION: LIFELINE

ED time and Risk-adjusted in-hospital mortality

Direct EMS patients



In hospital mortality (rolling 12 months)



Study Design

IMPROVE-IT

Patients stabilized post ACS ≤ 10 days:
LDL-C 50–125*mg/dL (or 50–100**mg/dL if prior lipid-lowering Rx)

*3.2mM
**2.6mM

N=18,144

Standard Medical & Interventional Therapy

Simvastatin 40 mg

Uptitrated to Simva 80 mg if LDL-C > 79 (adapted per FDA label 2011)

Ezetimibe / Simvastatin 10 / 40 mg

Follow-up Visit Day 30, every 4 months

90% power to detect ~9% difference

Duration: Minimum 2 ½-year follow-up **(at least 5250 events)**

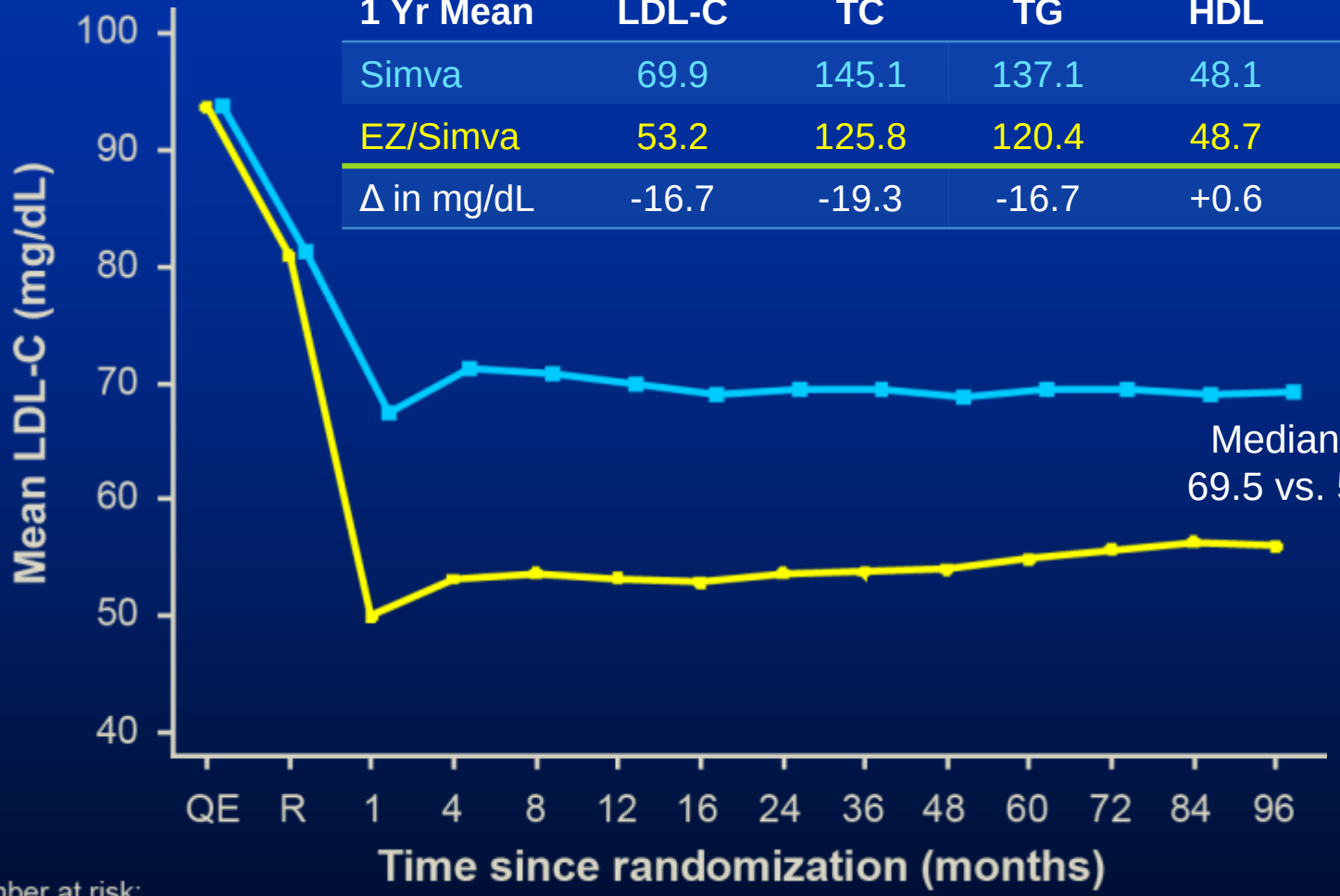
Primary Endpoint: CV death, MI, hospital admission for UA, coronary revascularization (≥ 30 days after randomization), or stroke

Cannon CP AHJ 2008;156:826-32; Califf RM NEJM 2009;361:712-7; Blazing MA AHJ 2014;168:205-12

LDL-C and Lipid Changes

IMPROVE-IT

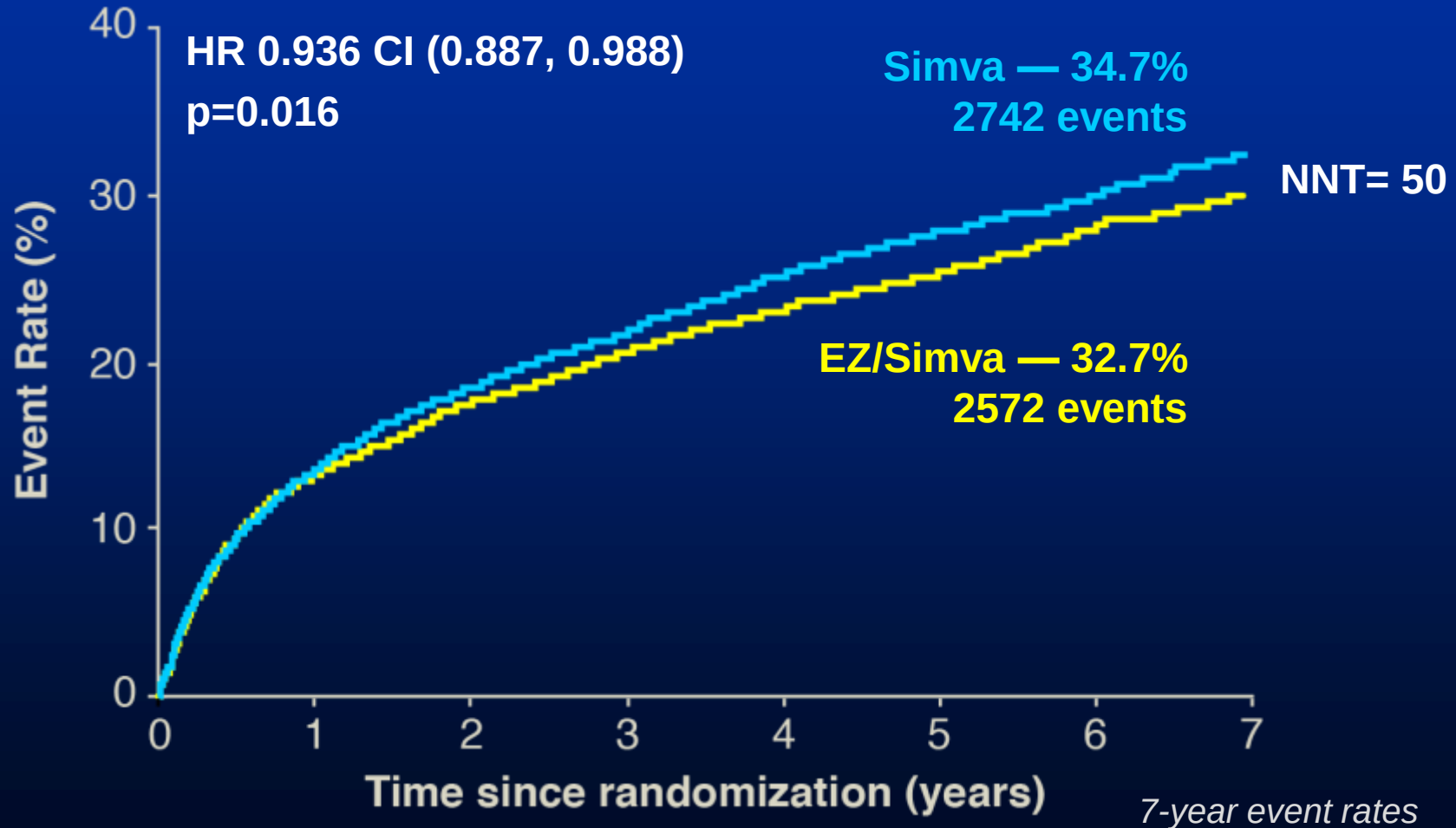
1 Yr Mean	LDL-C	TC	TG	HDL	hsCRP
Simva	69.9	145.1	137.1	48.1	3.8
EZ/Simva	53.2	125.8	120.4	48.7	3.3
Δ in mg/dL	-16.7	-19.3	-16.7	+0.6	-0.5



Median Time avg
69.5 vs. 53.7 mg/dL

Primary Endpoint — ITT

Cardiovascular death, MI, documented unstable angina requiring rehospitalization, coronary revascularization (≥30 days), or stroke



7-year event rates

Muchas Gracias

por vuestra atención