

MAYO CLINIC AND TORINO A 14 YEARS LONG STORY



Sebastiano Marra FESC , Emeritus Director of Cardiology .
Città della Salute e della Scienza TORINO

PRESIDENT
MAURO RINALDI

CO-PRESIDENTS
SEBASTIANO MARRA
FIORENZO GAITA

GIORNATE CARDIOLOGICHE **TORINESI**

TURIN,
October
25th-27th
2018

Starhotels Majestic



**A BRIDGE
OVER THE
ATLANTIC**

1st JOINT MEETING WITH MAYO CLINIC

1st Turin Cardiovascular Nursing Convention

**Acute coronary syndromes:
a bridge over the Atlantic**

Turin

October 28 - 29, 2005

Centro Congressi Lingotto - Via Nizza, 280 - Torino

PROGRAMMA DEFINITIVO e RACCOLTA ABSTRACT

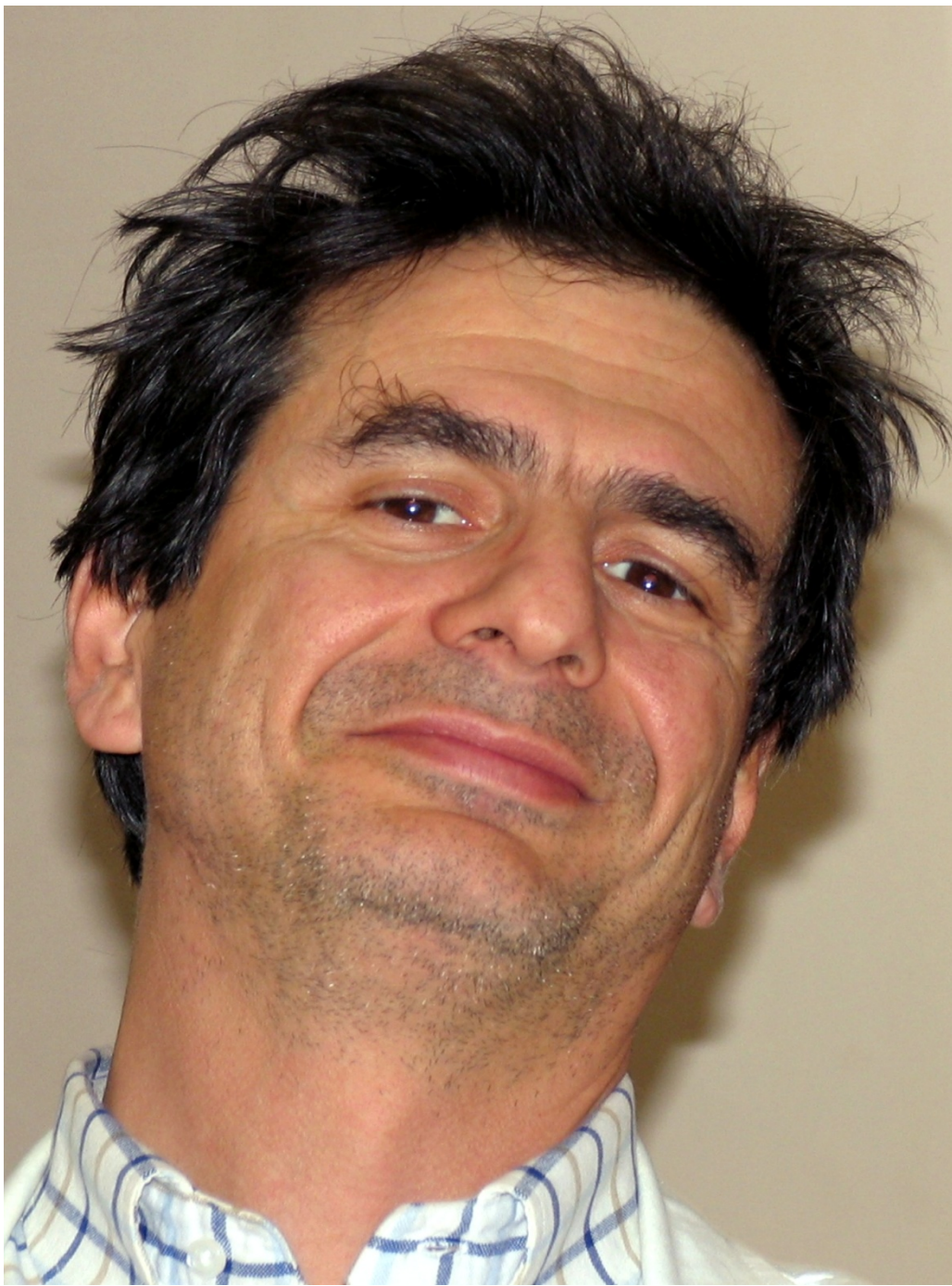
Regione Piemonte



Azienda Ospedaliera
San Giovanni Battista di Torino



MAYO CLINIC



Ciao !
Marco

NSTEMI : Strategies,Perspectives

Early Medical Therapy ?

Early Invasive Therapy

STEMI : Optimal Management

What is Optimal PCI ?

Facilitated PCI ?

Lytic ?

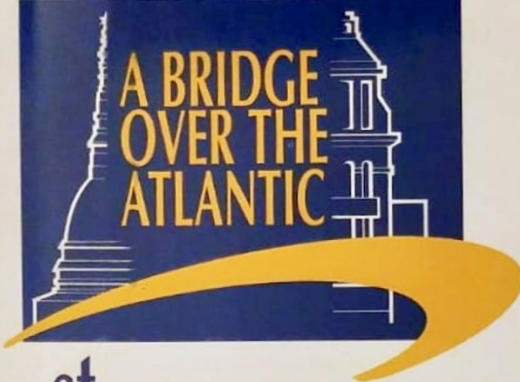
STEMI CELL THERAPY :

A New Therapeutic Approach:

Stem cells ?

Cytokines ?

STEMI COMPLICATIONS



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MAYO CLINIC

PRE HOSPITAL MANAGEMENT of STEMI

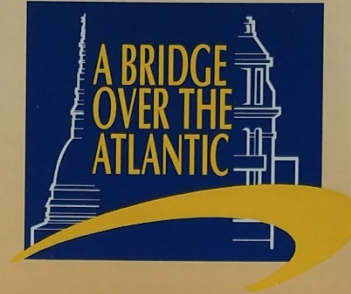
RESCUE PCI

D E S in ACUTE CORONARY SYNDROMES

DIABETIC PATIENTS

ELDERLY PATIENTS

USA and ESC GUIDELINES

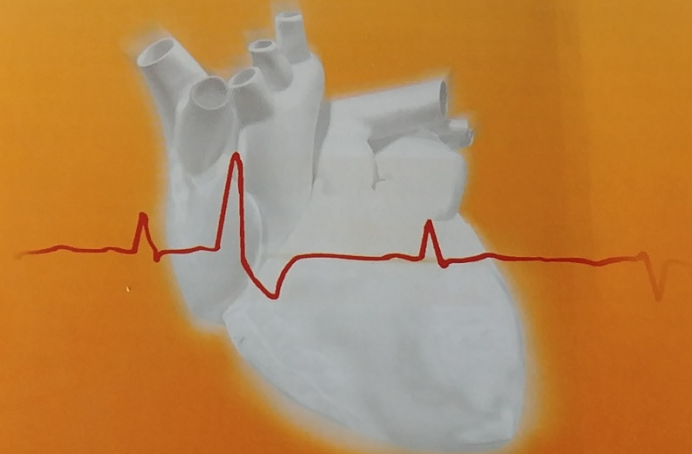


2nd Joint Meeting with Mayo Clinic
2nd Turin Cardiovascular Nursing Convention

ACUTE MYOCARDIAL INFARCTION

Torino, 2nd-4th November 2006

Final Program





TURIN, 20TH—21ST NOVEMBER 2008

GREAT INNOVATIONS IN CARDIOLOGY

4TH JOINT MEETING WITH MAYO CLINIC

4TH TURIN CARDIOVASCULAR NURSING CONVENTION



What's New on Adult Stem Cells?

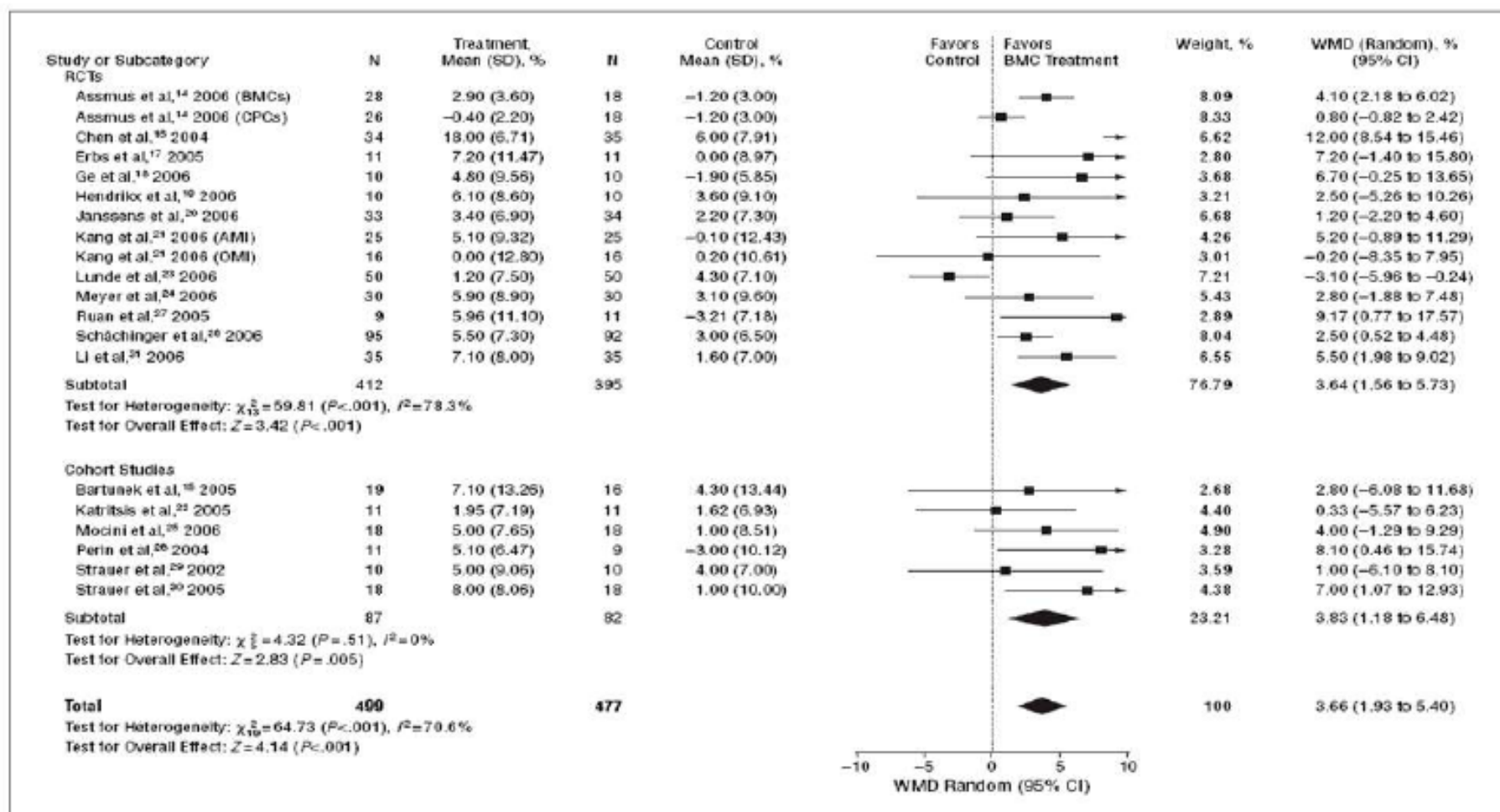
Jozef Bartunek

Cardiovascular Center, Aalst, Belgium

Faculty of Biomedical Engineering, TU Eindhoven, NL

**4th Joint Mayo Clinic-Torino Meeting
November 20-21, 2008**

Adult Stem Cells Therapy for Cardiac Repair



Overall clinical safety was demonstrated over 1 to 2 years period

Functional efficacy is only modest

Abdel-Latif, Arch Intern Med 2007



When does a Risk Marker becomes a Risk Factor?

Amir Lerman, MD
Professor of Medicine
Cardiovascular Division
Mayo Clinic, Rochester, MN

Lipoprotein-Associated Phospholipase A₂ Is an Independent Marker for Coronary Endothelial Dysfunction in Humans

Eric H. Yang, Joseph P. McConnell, Ryan J. Lennon, Gregory W. Barsness, GERALYN PUMPER, Stacy J. Hartman, Charanjit S. Rihal, Lilach O. Lerman, Amir Lerman

Objective—The purpose of the current study was to determine whether lipoprotein-associated phospholipase A₂ (Lp-PLA₂) is associated with coronary endothelial dysfunction and is a predictor of endothelial dysfunction in humans.

Methods and Results—Patients (172) with no significant coronary artery disease (<30% stenosis) undergoing assessment of coronary endothelial function were studied. Endothelial function was assessed by the change in coronary blood flow and coronary artery diameter in response to intracoronary acetylcholine. Plasma concentrations of Lp-PLA₂ were measured, and patients were divided into tertiles. Patients in tertiles 2 and 3 had a significantly lower change in coronary blood flow (63.8 ± 73.2 and 32.0 ± 71.7 versus $78.4 \pm 73.2\%$; $P < 0.001$) and greater epicardial coronary artery vasoconstriction (-14.1 ± 14.7 and -23.3 ± 25.1 versus $-9.5 \pm 15.2\%$ mean diameter change; $P < 0.001$) in response to acetylcholine. Patients with coronary endothelial dysfunction had significantly higher serum concentrations of Lp-PLA₂ than those with normal endothelial function (246.2 ± 71.6 versus 209 ± 56.7 ng/mL; $P = 0.001$). The odds ratio for coronary endothelial dysfunction in patients with Lp-PLA₂ in the highest tertile was 3.3 (95% CI, 1.6 to 6.6).

Conclusions—Lp-PLA₂ is independently associated with coronary artery endothelial dysfunction and is a strong predictor of endothelial dysfunction in humans. (*Arterioscler Thromb Vasc Biol.* 2006;26:106-111.)

Conclusions – Lp-PLA₂ is independently associated with coronary artery endothelial dysfunction and is a strong predictor of endothelial dysfunction in humans. (Arterioscler Thromb Vasc Biol, 2006;26:106-111.)

2009 Great Innovations in Cardiology JMMC

**5th Joint Meeting with Mayo Clinic
October 2009**

What happened to the clotting problem of DES?

**Malcolm Bell MBBS, FRACP
Professor of Medicine
Mayo Clinic
Rochester, MN. USA**

DES vs BMS in STEMI

2008 Meta-analysis

	DES vs BMS	
	Hazard ratio	<i>P</i> value
Reintervention (TLR)	0.36 (0.28-0.47)	<0.0001
Stent thrombosis	0.76 (0.47-1.23)	NS
Death	0.91 (0.66-1.08)	NS
Recurrent MI	0.85 (0.58-1.23)	NS

Favors DES (NNT = 13)

5th Joint Meeting with Mayo Clinic
15 -16 october 2009 Turin Italy

Mitral Valve Repair State of Art

Gian Paolo Ussia, MD, FSCAI



University of Catania

Division of Cardiology

Ferrarotto Hospital - Catania - ITALY



European & REALISM Experience

	Europe	REALISM
Patient Treated	219	128
Hospitals/Sites	19	26
Etiology: FMR/DMR (%)	72%/28%	60%/40%
Average Device Time (hr)	1:58	2:03
Clip Implant Rate (%)	96%	92%
1 Clip/2 Clip (%)	71%/29%	64%/36%
Site Reported MR Reduction (%) (in patients receiving a Clip)	98%	100%
Clip Embolization (%)	0%	0%



Torino

6° Joint meeting with Mayo Clinic

Great Innovation in Cardiology

14-15 Ottobre 2010

***Optimal antiplatelet and anticoagulant therapy for
patients treated in STEMI network***



Diego Ardissino

Parma

New European Guidelines 2010

STEMI

STEMI			
Antiplatelet therapy			
	ASA	I	B
	Clopidogrel ^f (with 600 mg loading dose as soon as possible)	I	C
	Prasugrel ^d	I	B
	Ticagrelor ^d	I	B
	+ GPIIb-IIIa antagonists (in patients with evidence of high intracoronary thrombus burden)		
	Abciximab	IIa	A
	Eptifibatide	IIa	B
	Tirofiban	IIIb	B
	Upstream GPIIb-IIIa antagonists	III	B
Anticoagulation			
	Bivalirudin (monotherapy)	I	B
	UFH	I	C
	Fondaparinux	III	B

Patient Selection for TAVI: The US Perspective

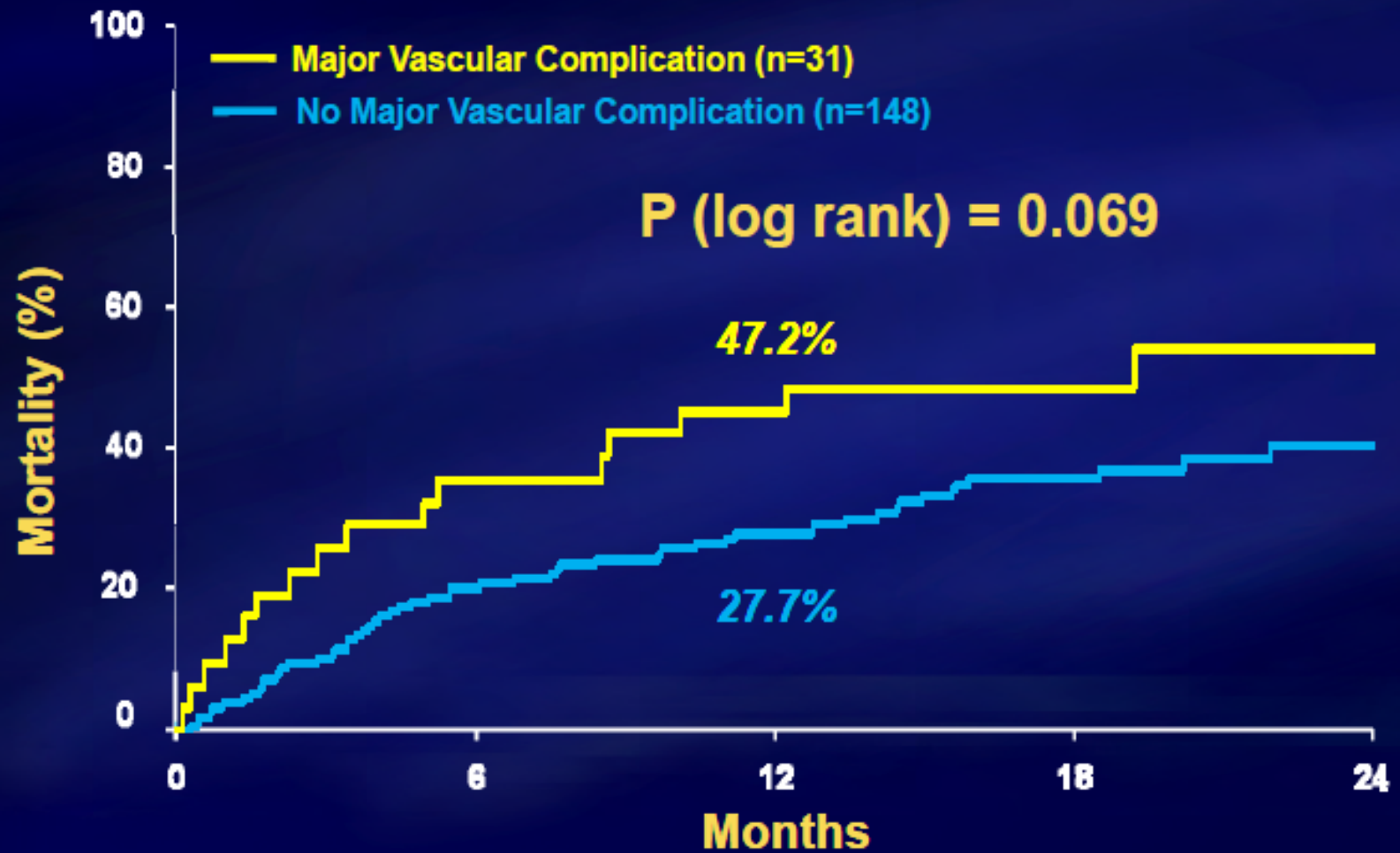
Charanjit S. Rihal MD MBA
Professor of Medicine
Chair, Division of
Cardiovascular Diseases

Mayo Clinic and Foundation
Rochester, MN, USA



Mortality vs. Major Vasc Complications

TAVI patients





What is new in the Treatment of STEMI?

Malcolm R. Bell, MBBS
Mayo Clinic
Rochester, MN

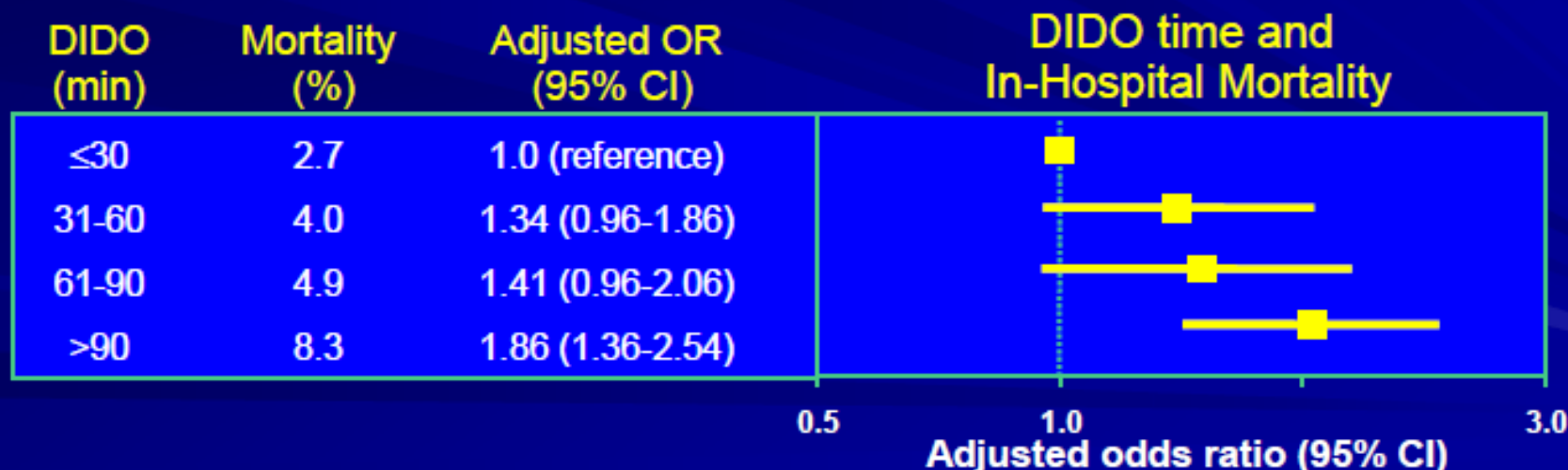
October 2011

DIDO and In Hospital Mortality

NCDR ACTION Registry-GWTG

DIDO ≤ 30 min
2.7% mortality

DIDO >30 min
5.9% mortality

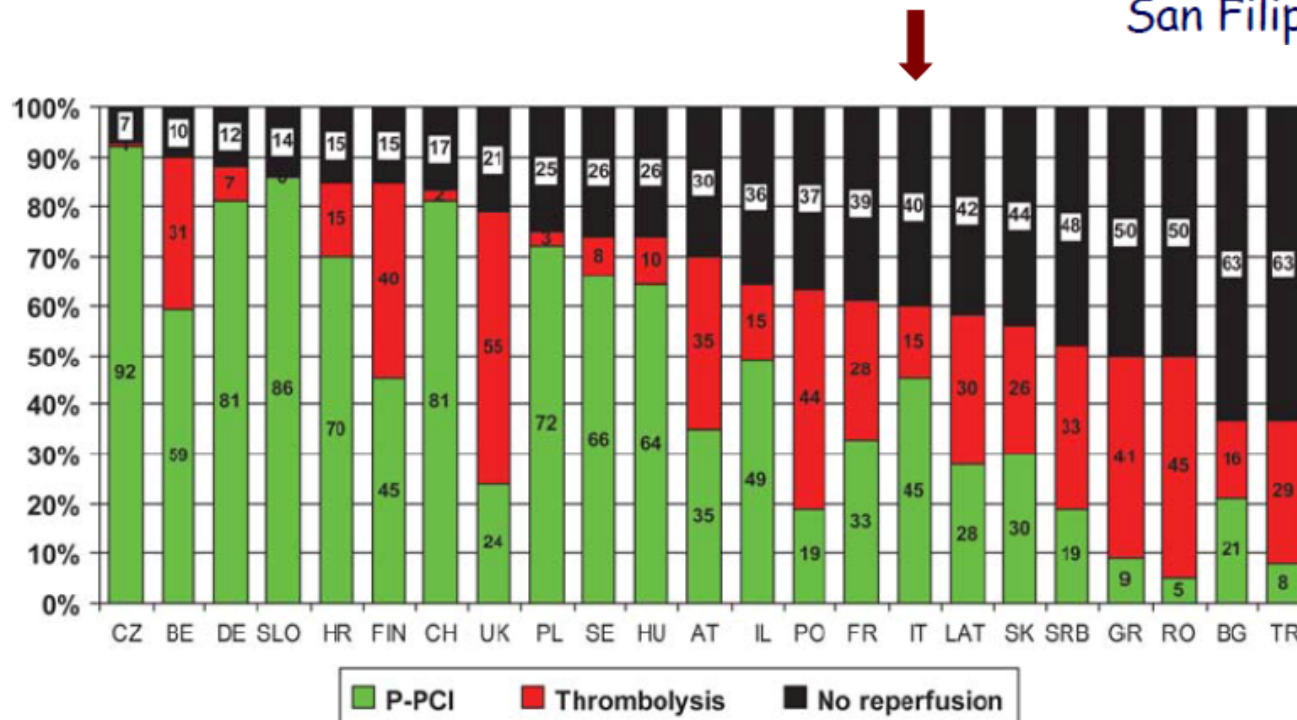


STEMI networking in Europe and Italy

Marco Tubaro, MD FESC

STEMI reperfusion treatment in Europe

ICCU - Cardiovascular Department
San Filippo Neri Hospital, Rome (IT)



GREAT INNOVATIONS IN CARDIOLOGY

6TH JOINT MEETING
WITH MAYO CLINIC

14TH -15TH October 2010
TORINO, Italy



RETE INFARTO -STEMI

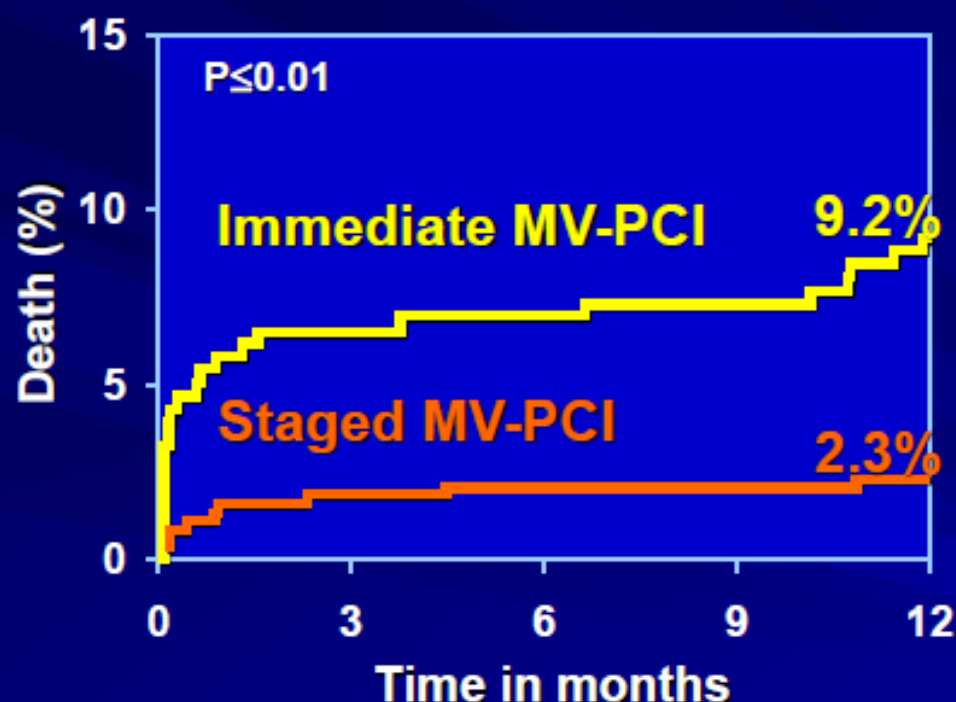
Non solo angioplastica primaria ma....

- Epidemiologia che cambia
- Efficienza dell'ECG pre-ospedaliero
- Ruolo dell'organizzazione del 118
- Terapia ottimale preparatoria all'angioplastica
- Non basta la ricanalizzazione della coronaria...ma è necessaria la riperfusione del muscolo cardiaco



Immediate vs Staged Multivessel PCI

HORIZONS-AMI Trial



Staged MV-PCI

Median 30-days

Immediate MV-PCI

- ↑ mortality
- ↑ cardiac mortality
- ↑ stent thrombosis
- ↑ bleeding

Independent predictor
of 1-yr mortality

Kornowski R: JACC 2011



Università degli Studi di Torino
Ospedale San Giovanni Battista - Molinette



Trans-Apical Aortic valve implantation in Italy and in Europe

TAVI Heart Team

Prof. Mauro Rinaldi

Prof. Fiorenzo Gaita

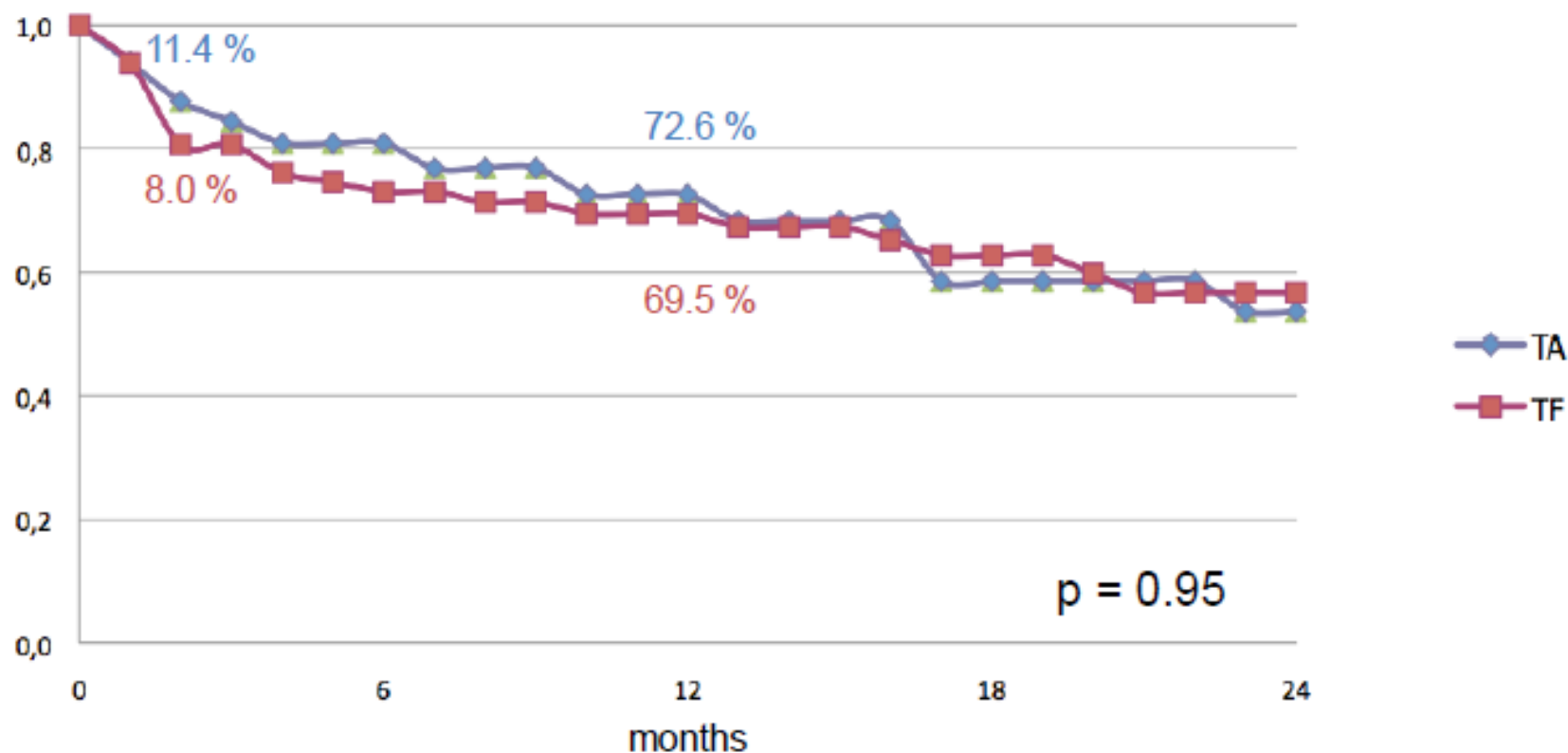
Dott. Sebastiano Marra

Torino Experience (110 patients)

TA LogES 24.7 ± 12.1 %

TF LogES 20.2 ± 12.0 %

$p = 0.07$



Number
at risk

35

75

18

34

11

17

'AF Begets AF'

The Role of Early Action

Maurits A. Allesie

Department of Physiology

Cardiovascular Research Institute

Maastricht, The Netherlands

In Patients with Longstanding AF
the Atria have been Transformed
into a **Double Layer** of
Dissociated Muscle Bundles

Antithrombotic therapies in ACS

year 2007

- aspirin
- clopidogrel
- GPIIb/IIIa RB
- UFH
- enoxaparin

year 2012

- aspirin
- clopidogrel
- prasugrel
- ticagrelor
- GPIIb/IIIa RB
- UFH
- enoxaparin
- fondaparinux
- bivalirudin

year 2014

- aspirin
- clopidogrel
- prasugrel
- ticagrelor
- vorapaxar
- GPIIb/IIIa RB
- cangrelor
- rivaroxaban
- UFH
- enoxaparina
- fondaparinux
- bivalirudina

Antiplatelet
Anticoagulant

Contemporary recommendations on Antiplatelet therapy in NSTEMACS PCI

NSTEMACS				
Antiplatelet therapy				
	ASA	I	C	—
	Clopidogrel (with 600 mg loading dose as soon as possible)	I	C	—
	Clopidogrel (for 9–12 months after PCI)	I	B	55
	Prasugrel ^d	IIa	B	246,247
	Ticagrelor ^d	I	B	248
	+ GPIIb–IIIa antagonists (in patients with evidence of high intracoronary thrombus burden)			
	Abciximab (with DAPT)	I	B	249
	Tirofiban, Eptifibatide	IIa	B	55
	Upstream GPIIb–IIIa antagonists	III	B	65



EUROPEAN
 SOCIETY OF
 CARDIOLOGY®

European Heart Journal
 doi:10.1093/eurheartj/ehq277

ESC/EACTS GUIDELINES



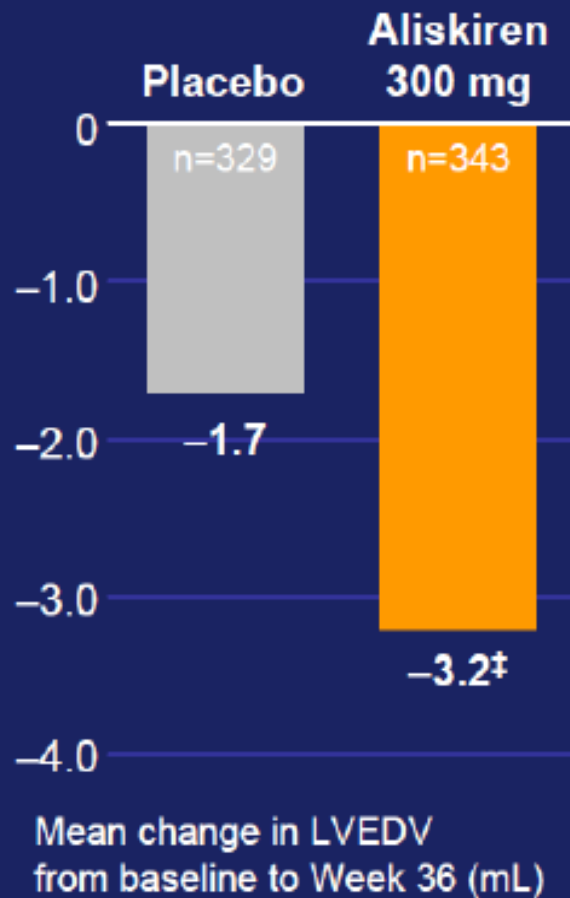
Advances in Cardiac Arrhythmias and Great Innovations in Cardiology

**Direct renin inhibition in patients with
heart failure: is it the missing piece of
the puzzle?**

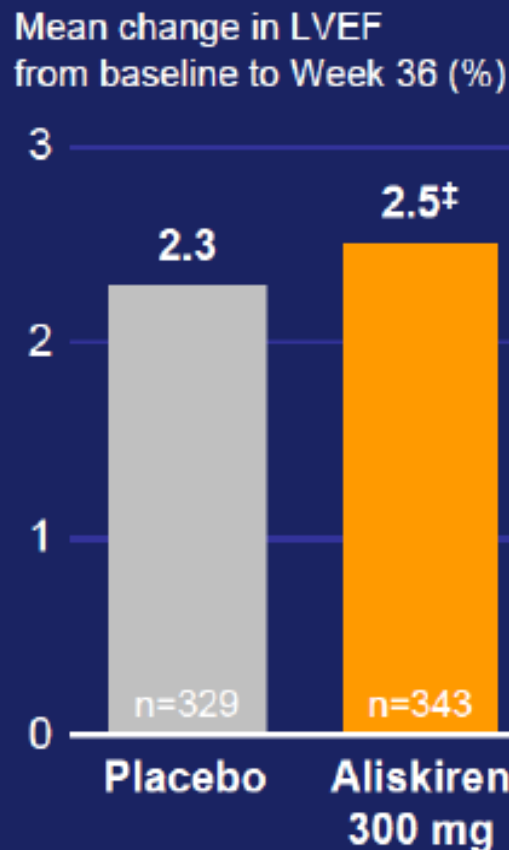
**Marco Metra
Cattedra e U.O. di Cardiologia
Università e Spedali Civili di
Brescia**

Aliskiren provided numerically, but not significantly, greater improvements in echocardiographic measures of LV dysfunction compared with placebo

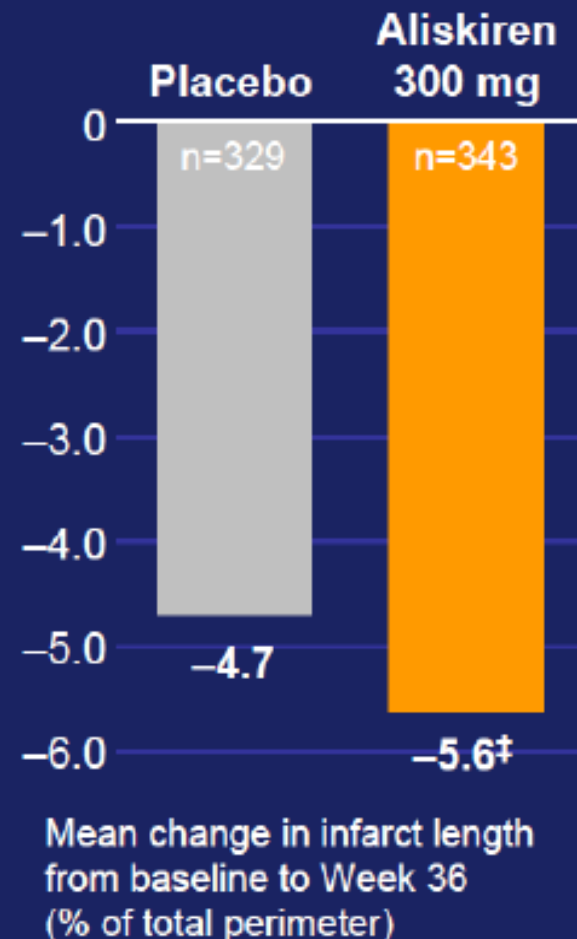
LVEDV



LVEF



Infarct length



[‡]p = non-significant vs placebo

LVEDV: study population baseline = ~132.4 mL; LVEF: study population baseline = ~37.8%

Infarct length: study population baseline values = ~24.8%

Data on file,
Novartis Pharma AG 2010

UNIVERSITA DEGLI STUDI DI MILANO



I.R.C.C.S. POLICLINICO SAN DONATO

CENTRO PER LO STUDIO E LA TERAPIA DELLE MALATTIE CARDIOVASCOLARI

“E. MALAN”

XXIV GIORNATE CARDIOLOGICHE TORINESI

**ADVANCES IN CARDIAC
ARRHYTHMIAS**

and

**GREAT INNOVATIONS
IN CARDIOLOGY**

Directors

Fiorenzo Gaita
Sebastiano Marra

Scientific Committee

Malcolm Bell, *Usa*
Martin Borggrefe, *Germany*
Amir Lerman, *Usa*
Jean Francois Leclercq, *France*
Dipen Shah, *Suisse*

Organization Committee

Carlo Budano, *Italy*
Davide Castagno, *Italy*
Monica Andriani, *Italy*

Turin

October 25-27, 2012



*Leadless ICD:
How far from real life?!*

Riccardo Cappato, MD

Pierpaolo Lupo, MD

Hussam Ali, MD

Sudden cardiac death in “healthy” heart

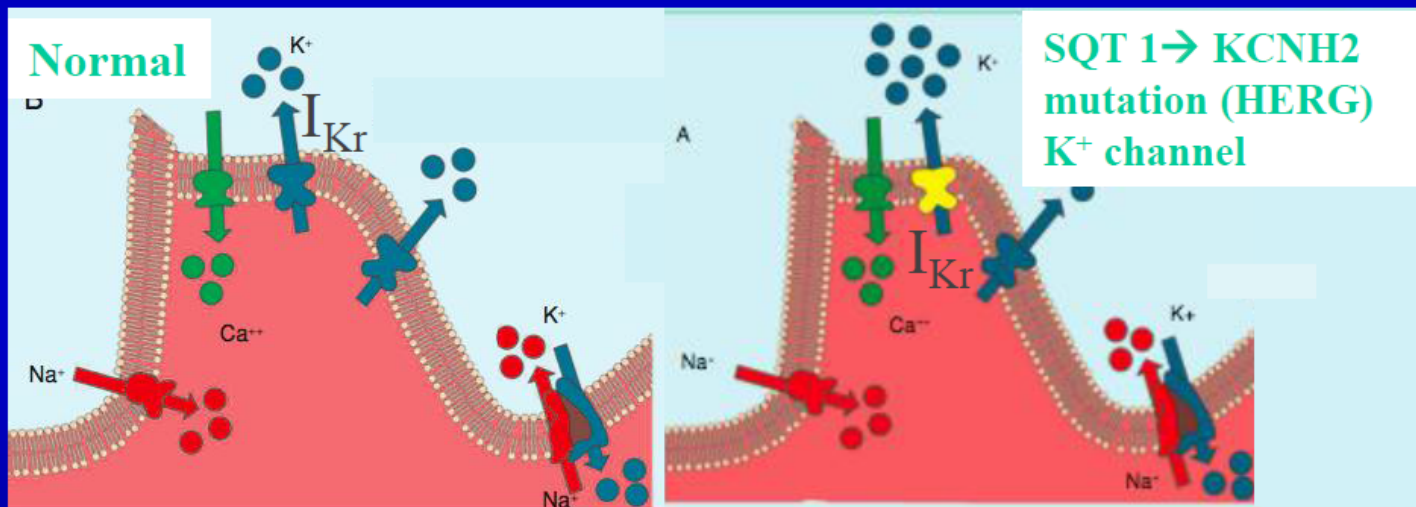
Torino, 27th September 2013

Prof. Fiorenzo Gaita

Director of the Cardiology School - University of Turin, Italy

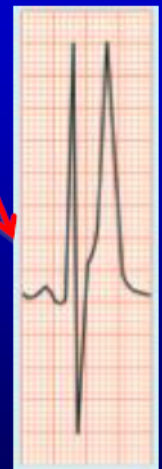
Sudden Death Associated With Short-QT Syndrome Linked to Mutations in HERG

Ramon Brugada, Kui Hong, Robert Dumaine, Jonathan Cordeiro, Fiorenzo Gaita, Martin Borggrefe, Teresa M. Menendez, Josep Brugada, Guido D. Pollevick, Christian Wolpert, Elena Burashnikov, Kiyotaka Matsuo, Yue Sheng Wu, Alejandra Guerchicoff, Francesca Bianchi, Carla Giustetto, Rainer Schimpf, Pedro Brugada and Charles Antzelevitch



I_{Kr} gain of function

Reduction of action potential duration and refractoriness



The background of the slide is a scenic photograph of a river flowing under a stone bridge. In the distance, a hillside town with a prominent domed church is visible under a clear blue sky. Two large, leafless trees frame the scene on the left and right sides.

EXTRACORPOREAL SHOCKWAVES MYOCARDIAL REVASCULARIZATION: AN EFFECTIVE TECHNOLOGY FOR MYOCARDIAL PERFUSION

**SEBASTIANO MARRA MD FESC
DIRETTORE**

**DIPARTIMENTO CARDIOVASCOLARE E TORACICO
CITTA' DELLA SALUTE E DELLA SCIENZA TORINO**

**ADVANCES IN CARDIAC
ARRHYTHMIAS
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Monica Andriani, *Italy*

Turin

September 27-28, 2013

*Centro Congressi
Unione Industriale*



Università degli Studi di Torino



Azienda Ospedaliera
Ca' Granda
Università di Milano

When to implant VAD in patients with heart transplantation indication

Aldo Cannata

Dept of Cardiac Surgery
Niguarda Ca' Granda Hospital
Milano

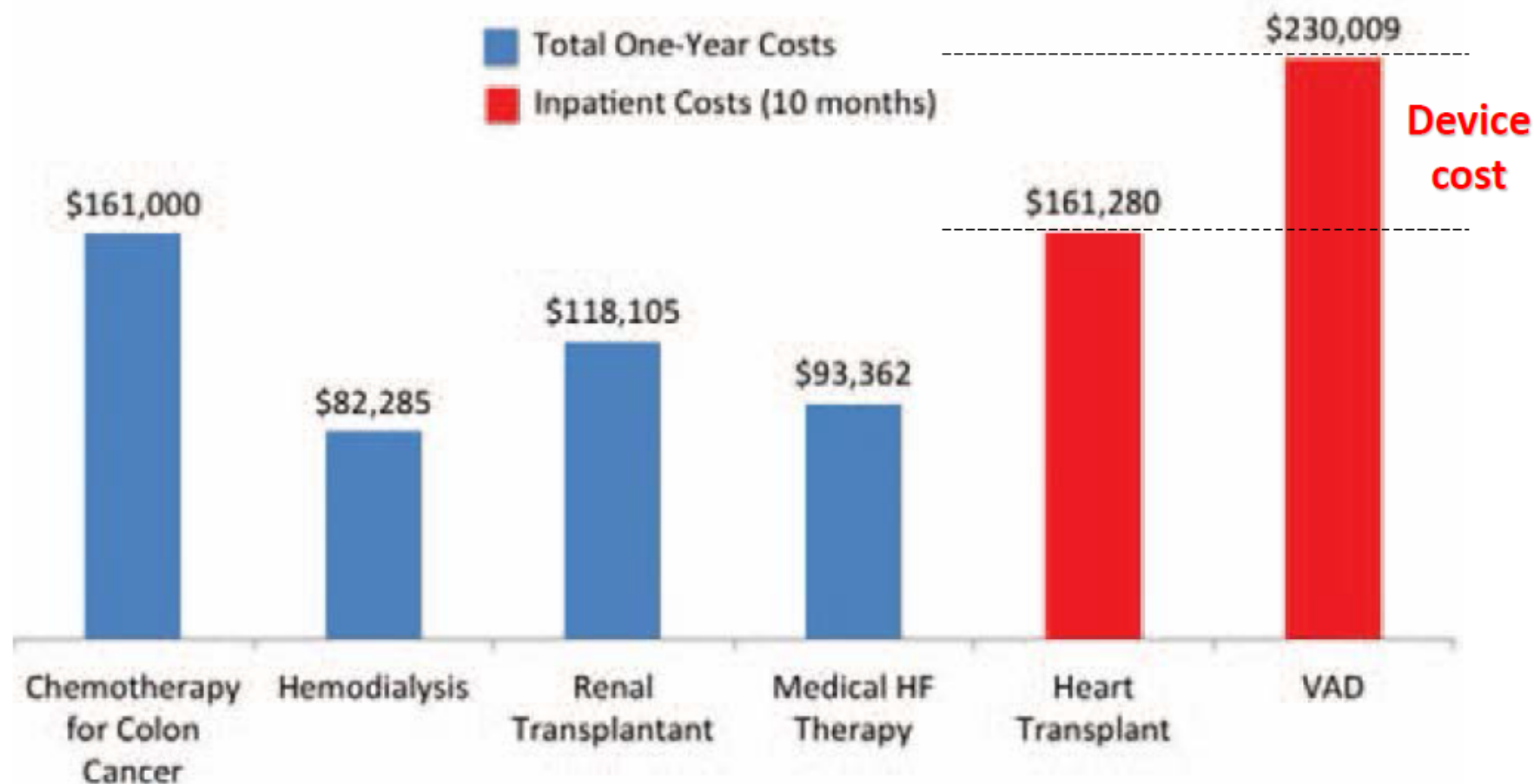
LVAD strategies

	In waiting list?	Goal
Bridge to transplant	Yes	To keep pts alive up to HTx
Bridge to candidacy	Not yet	To treat high PVR
Bridge to decision	Unknown	To keep pts alive for evaluation
Destination therapy	No	Definitive therapy
Bridge to recovery	Not yet	To allow myocardial recovery

Cost of Ventricular Assist Devices

Can We Afford The Progress?

Costs of Treating Advanced Stage Illness



ARE ALL NOVEL ORAL CREATED ANTICOAGULANTS EQUAL ?

✕ Evidence from the recent literature

Prof Alessandro Capucci
Direttore Clinica di Cardiologia
Università Politecnica delle Marche
Ancona

Cardioversion during Phase III trials

Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart
Association

Learn and Live™

Dabigatran Versus Warfarin in Patients With Atrial Fibrillation: An Analysis of Patients Undergoing Cardioversion

Rangadham Nagarakanti, Michael E. Chernick, Timothy H. Aikens, Greg Parekh, Paul A. Reilly, *Circulation* pt
DOI: 10.1161/CIR

Circulation is published by the American Heart Association
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Vol. 61, No. 19, 2013
ISSN 0735-1097/\$36.00
<http://dx.doi.org/10.1016/j.jacc.2013.02.025>

Heart Rhythm Disorders

Outcomes After Cardioversion and Atrial Fibrillation Ablation in Patients Treated With Rivaroxaban and Warfarin in the ROCKET AF Trial

Jonathan P. Piccini, MD, MHS,* Susanna R. Stevens, MS, Manesh R. Patel, MD,* Jonathan L. Halperin, MD,† Dani Graeme J. Hankey, MD,§ Werner Hacke, MD, PhD,|| Ric Christopher C. Nessel, MD,¶ Kenneth W. Mahaffey, MD, Robert M. Califf, MD,** Günter Breithardt, MD†† for the &c Investigators

Durham, North Carolina; New York, New York; Boston, Mass; Heidelberg and Münster, Germany; Raritan, New Jersey; and

Journal of the American College of Cardiology
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Vol. 63, No. 11, 2014
ISSN 0735-1097/\$36.00
<http://dx.doi.org/10.1016/j.jacc.2013.09.062>

Antithrombotic Therapy

Efficacy and Safety of Apixaban in Patients After Cardioversion for Atrial Fibrillation

Insights From the ARISTOTLE Trial
(Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation)

Greg Flaker, MD,* Renato D. Lopes, MD, PhD,† Sana M. Al-Khatib, MD, MHS,† Antonio G. Hermosillo, MD,‡ Stefan H. Hohnloser, MD,§ Brian Tinga, MS,† Jun Zhu, MD,|| Puneet Mohan, MD, PhD,¶ David Garcia, MD,‡ Jozef Bartunek, MD, PhD,** Dragos Vincereanu, MD, PhD,†† Steen Husted, MD, DMSc,‡‡ Veli Pekka Haajola, MD, PhD,§§ Marten Rosengqvist, MD,||| John H. Alexander, MD, MHS,† Christopher B. Granger, MD,† for the ARISTOTLE Committees and Investigators

Columbia, Missouri; Durham, North Carolina; Tlalpam, Mexico; Frankfurt, Germany; Beijing, China; Princeton, New Jersey; Albuquerque, New Mexico; Aalst, Belgium; Bucharest, Romania; Århus, Denmark; Helsinki, Finland; and Stockholm, Sweden





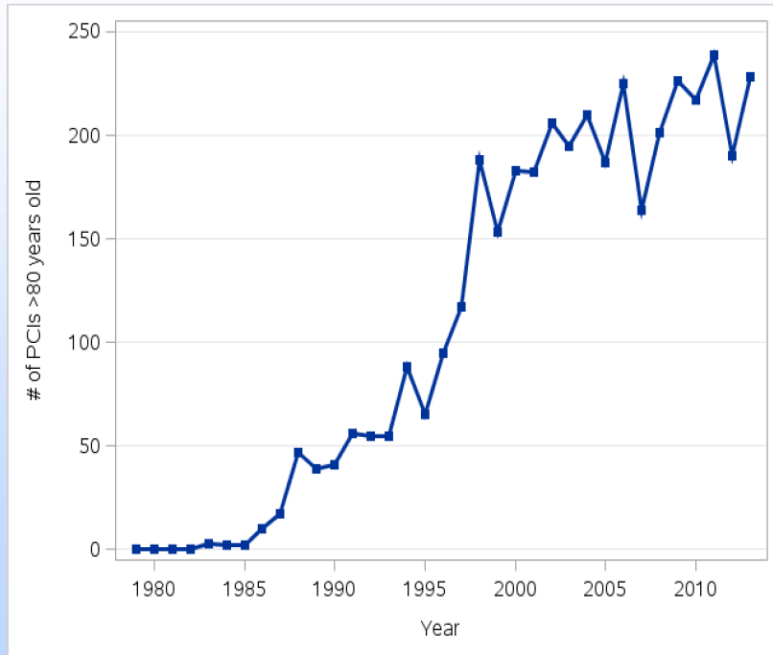
Torino, IT
October 2015



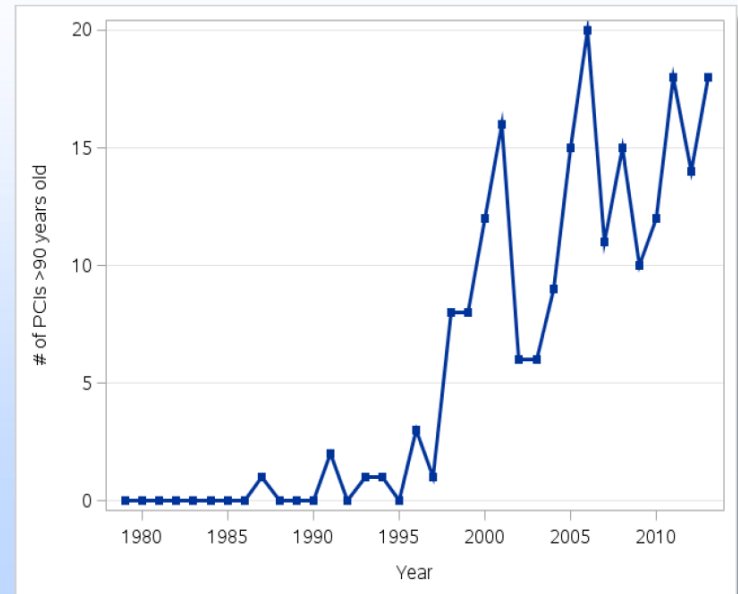
PCI in the Older Patient

Malcolm R. Bell, MBBS, FRACP
Director Ischemic Heart Disease Program
Mayo Clinic, MN, USA

Mayo Clinic: PCI in Octogenarians

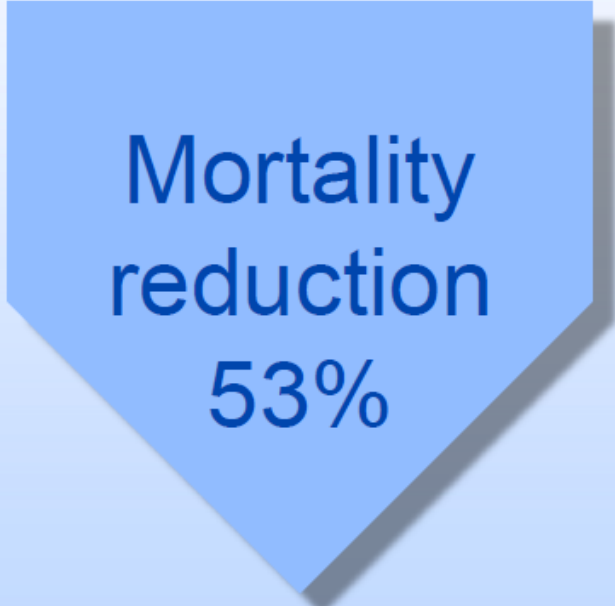


Mayo Clinic: PCI in Nonagenarians



STEMI in 33,644 Nonagenarians

PCI use



Mortality
reduction
53%

NNT <10 patients



Percutaneous Left Atrial Appendage Occlusion in Patients With Non-valvular Atrial Fibrillation – Are Indications Expanding?

Paul A. Friedman, MD

Mayo Clinic
Rochester, MN, USA

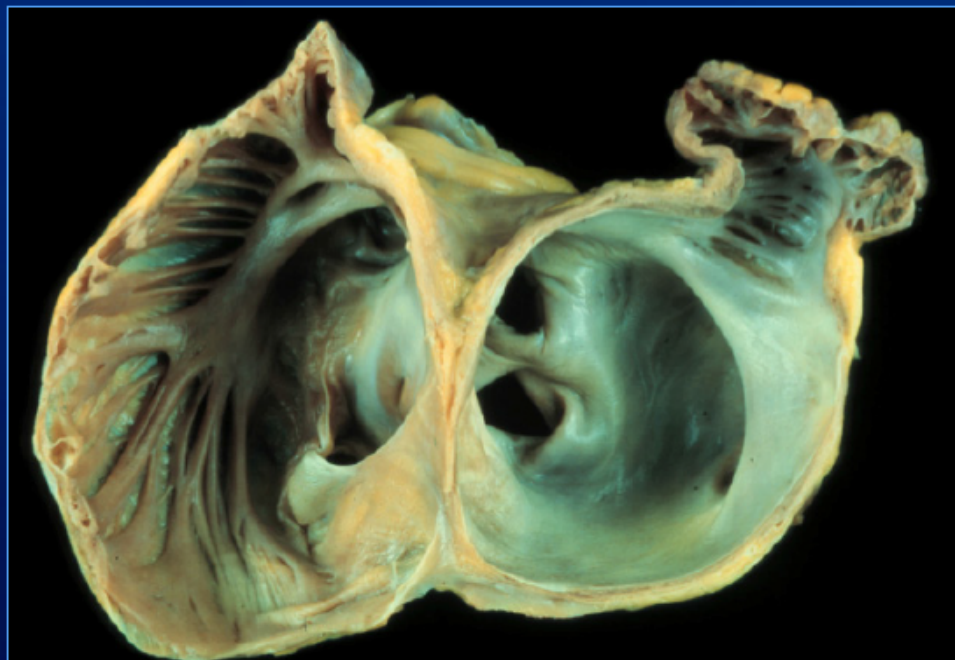
Anticoagulants – Tested in Trials With >60,000 Patients for Stroke Prevention

Bleeding rates

- Major 2-3 %
- Any 15-25%

Discontinuation rates

- 20-25% in major studies

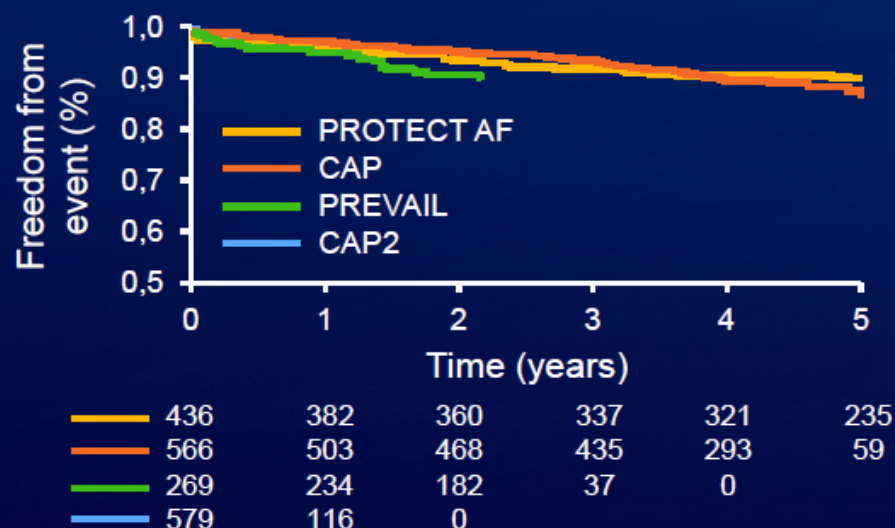
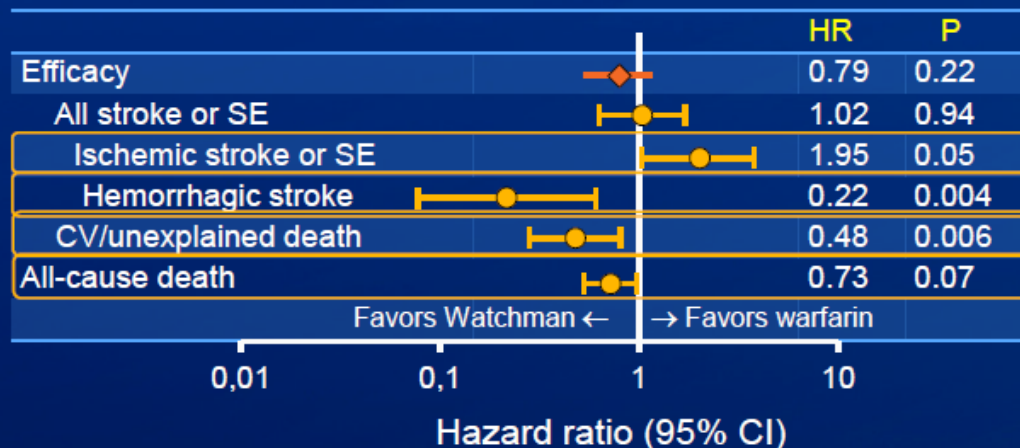
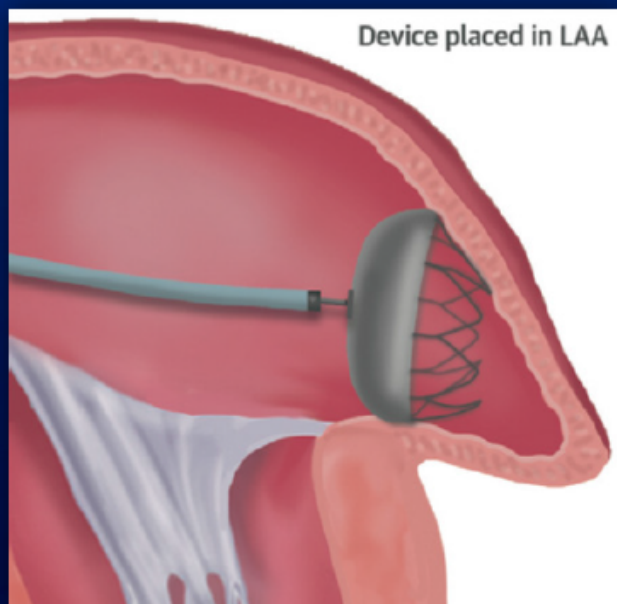


Concept: Avoid “systemic” complications by using “local” approach: & 100% adherence

Possibly control AF?

LAA Closure: Patient-Level Meta-Analysis

Stroke Prevention in Nonvalvular Atrial Fibrillation With LAA Closure



ADVANCES IN CARDIAC ARRHYTHMIAS AND GREAT INNOVATIONS IN CARDIOLOGY

Torino, October 13 – 15, 2016

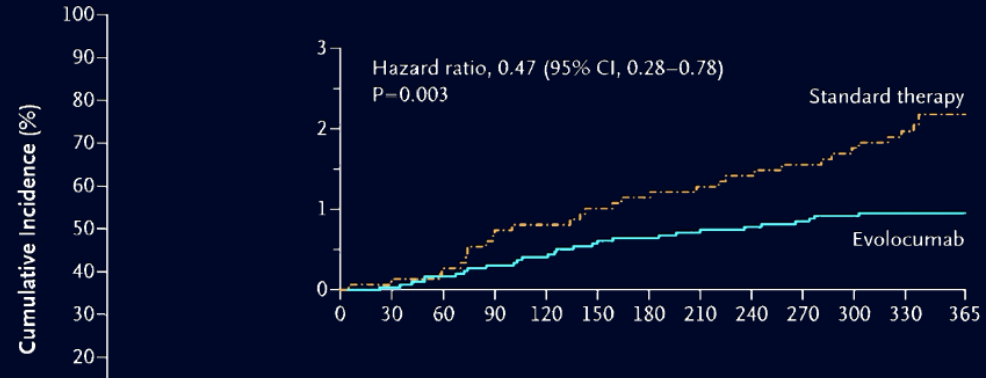
**PCSK9 INHIBITORS: A HUGE LITERATURE,
NOW WE ARE READY TO USE THEM**



Pasquale Perrone Filardi
Federico II University of Naples, Italy

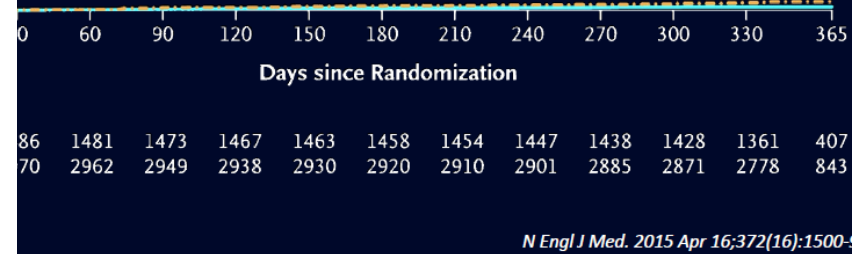
Cumulative Incidence of Cardiovascular Events

Included among the cardiovascular events were death, myocardial infarction, unstable angina requiring hospitalization, coronary revascularization, stroke, transient ischemic attack, and hospitalization for heart failure. Cardiovascular events were reported in 29 of 2976 patients in the evolocumab group (Kaplan–Meier 1-year event rate, 0.95%) and in 31 of 1489 patients in the standard-therapy group (Kaplan–Meier 1-year event rate, 2.18%). The inset shows the same data on an expanded y axis. The P value was calculated with the use of a log-rank test



PCSK9 inhibitor upcoming CVOTs

Mnf/ Molecule	Main trial	Patients & Inclusion criteria	Comparator	Primary CV Outcome	Expected Lipid Reduction†
Amgen Evolocumab AMG 145	FOURIER Phase III Recruiting Trial results Q1 2017	28 000 • History of a prior CV event or PAD and at high risk for a recurrent event • Fasting LDL-C ≥ 70 mg/dL or non-HDL-C ≥ 100 mg/dL on a background of atorvastatin • Fasting triglycerides ≤ 400 mg/dL	Statin + AMG 145 vs. Statin + placebo	Time to first of: - cardiovascular death - myocardial infarction - hospitalization for unstable angina, stroke, or coronary revascularization	~65% LDL-C reduction
Sanofi/Regeneron Alirocumab (REGN 727)	ODYSSEY Phase III Recruiting Trial results Q1 2018	18 000 • Recently hospitalized for ACS • >40 yrs recently hospitalized for ACS event (4-52 wks post ACS event) • >70mg/dL on background of atorvastatin, rosuvastatin, or with demonstrated statin intolerance	Statin + REGN 727 vs. Statin + placebo	Occurrence of CV events -composite endpoint consisting of: - coronary heart disease death - non-fatal myocardial infarction - fatal/non-fatal ischemic stroke - unstable angina requiring hospitalization	~50% LDL-C reduction



N Engl J Med. 2015 Apr 16;372(16):1500-9

Global Mortality Reduction : A Cardiovascular Prevention Result

Sebastiano Marra
Fesc
president



**ADVANCES IN CARDIAC
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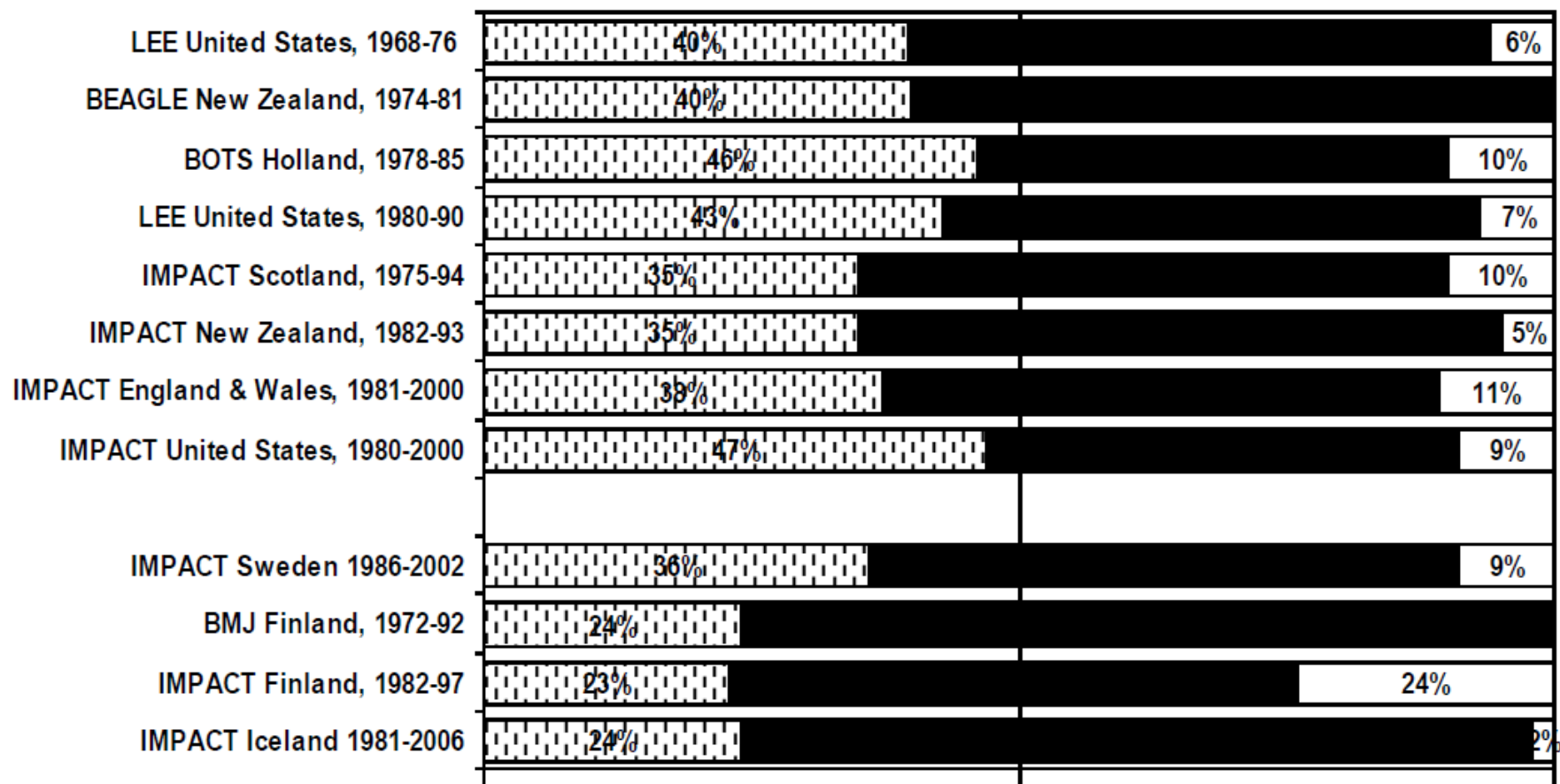
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Comparisons with other studies

% CHD mortality falls attributed to:

▨ Treatments ■ Risk factors □ Unexplained



STATE OF THE ART : Optimal Medical Therapy – Competing with or Complementary to Rivascularization in Patients with Coronary Artery Disease

J.Iqbal,R.Widmer,B.J.Gersh Eurointervention 2017 ; 13 : 751-759

LIFESTYLE MODIFICATIONS

Along with revascularisation and OMT, all cardiac patients should be encouraged to adopt a healthy lifestyle including healthy eating, regular physical activity and management of other cardiac risk factors. Patients who continue to smoke after revascularisation have poor long-term outcomes^{41,42}.

IN CONCLUSION.....

Bittner et al

have also shown that simultaneous control of multiple cardiovascular risk factors improves outcomes⁴⁰. There is definite room for improvement in patient education about lifestyle modifications and it should be an integral part of medical management⁴⁵.

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