Scientific Programme jointly organized with

ESC Council for Cardiology Practice

EUROPEAN SOCIETY OF CARDIOLOGY

Italian Council of Cardiology Practice

1st European Meeting of Cardiology Practice
Spring Meeting of the ESC Council
for Cardiology Practice

VIII Congresso Nazionale CFC
Collegio Federativo di Cardiologia - ICCP

OPEN DEBATES in CARDIOLOGY

(discussions on particular topics in a meeting
in which opposing arguments are put forward)

April 16th - 18th 2010

Hotel Royal Continental
NAPLES (Italy)

SYMPOSIUM

16.00 **Ranolazine: the novel agent to support symptomatic stable angina patients in maintaining their quality of life**
Ranolazina: un nuovo farmaco per migliorare la qualità della vita nei pazienti con angina stabile sintomatica
Chairman: F. Fedele (*Roma*), G. Barón Esquivas (*Siviglia*)

16.00 **Introduction**
Introduzione
G. Barón Esquivas (*Siviglia*)

16.05 **Understanding the pathophysiology of ischemic chronic disease: stable angina, the tip of the iceberg**
Approfondire la fisiopatologia della malattia ischemica cronica. Angina stabile, la punta dell'iceberg
F. Triposkiadis (*Grecia*)

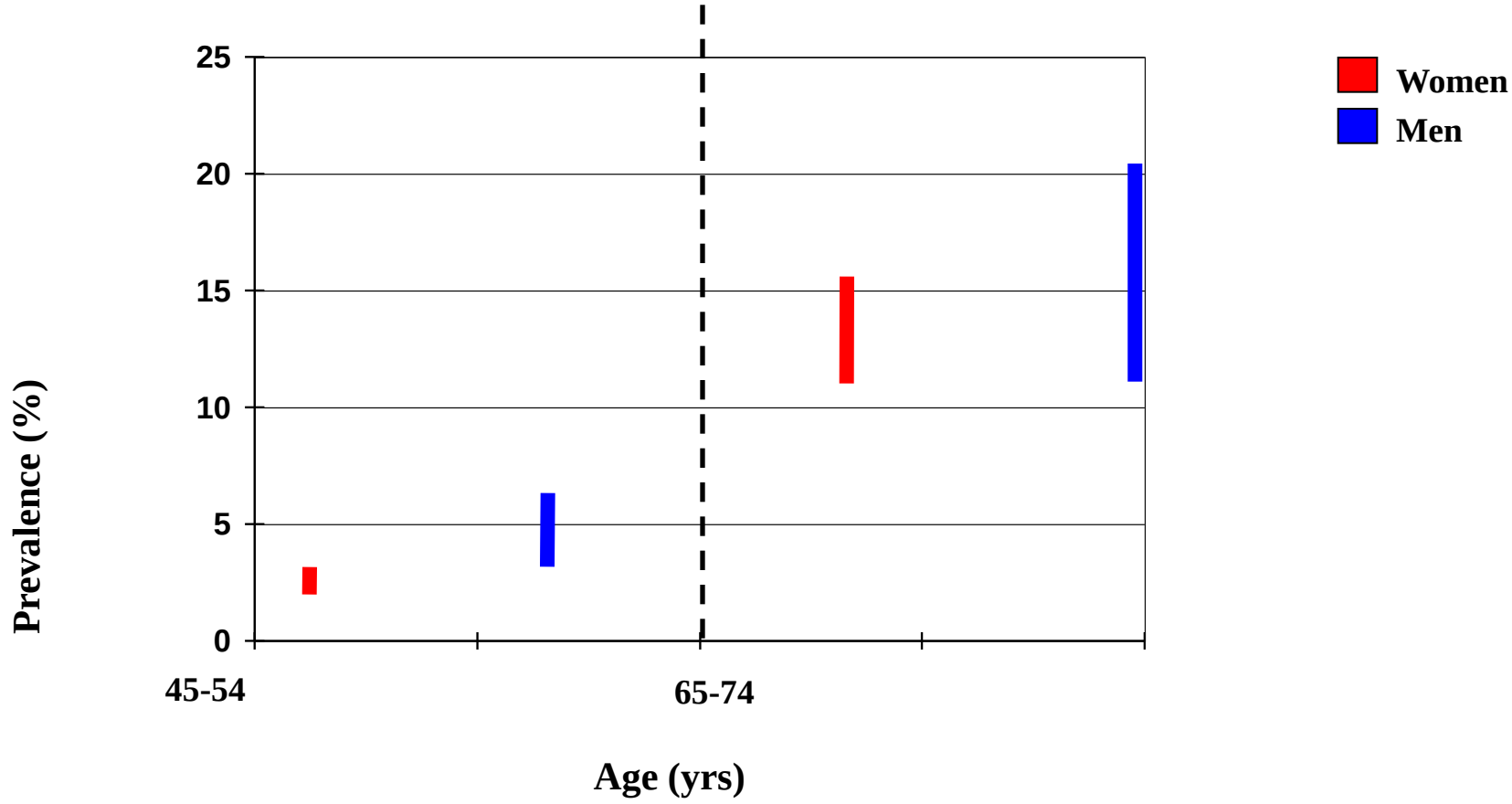
16.25 **Previous clinical conditions and comorbidities: need to optimize therapy**
Condizioni cliniche pregresse e comorbilità: bisogno di ottimizzare la terapia
F. Fedele (*Roma*)

16.45 **New mechanism of action: from late INa to O2 balance**
Nuovo meccanismo d'azione: dai canali tardivi del sodio al bilancio dell'ossigeno
G. Hasenfuss (*Germania*)

17.05 **From pharmacology to clinical practice**
Dalla farmacologia alla pratica clinica
P. Merlini (*Milano*)

17.25 **Conclusions**
Conclusioni
F. Fedele (*Roma*)

Prevalence of angina



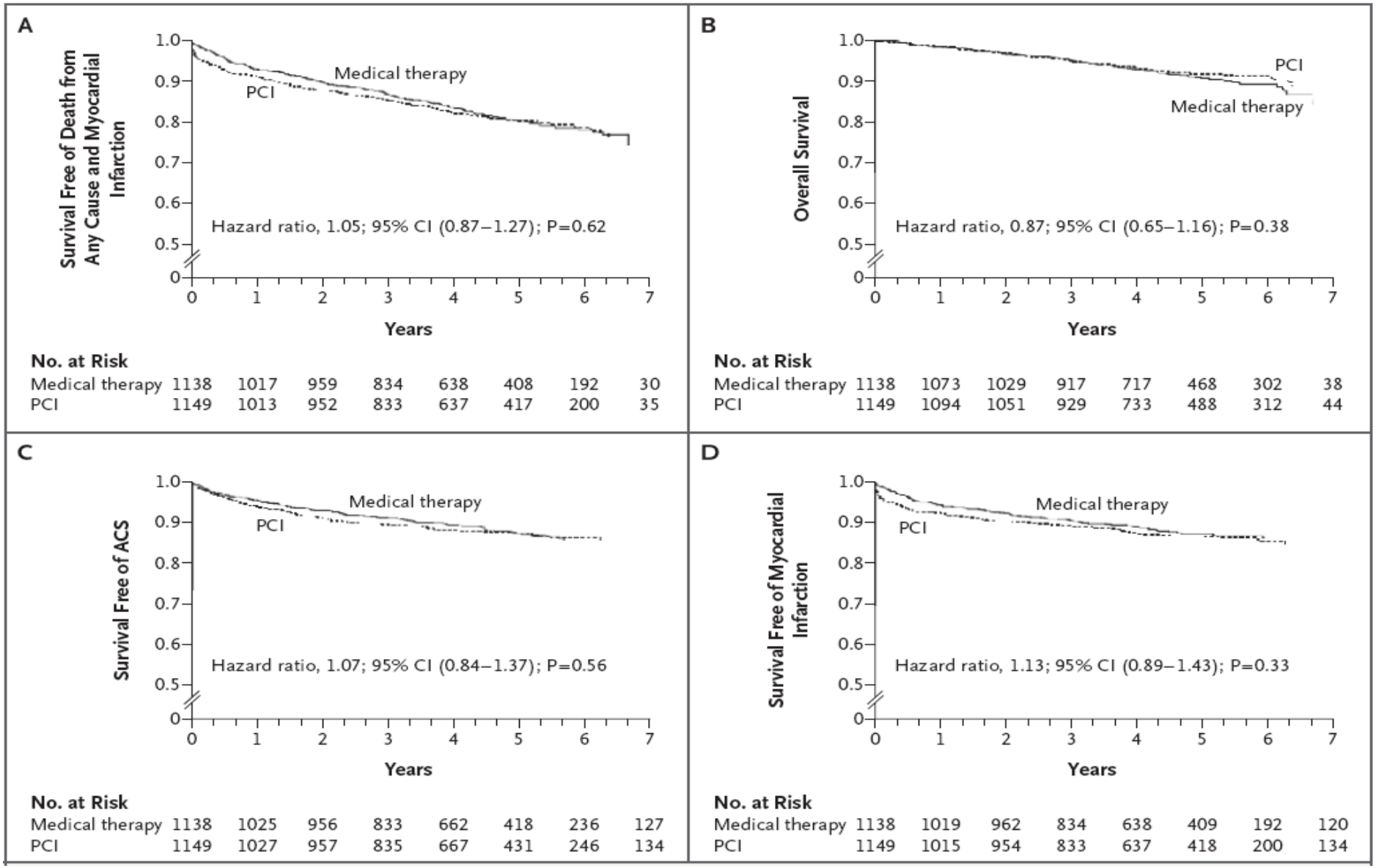
Guidelines of stable angina. Eur Heart J, 2006: 27: 1341-81

Table 2 The use of secondary preventive and antianginal medications in the Euro heart Survey of Stable angina at initial assessment, and the use of these mediations at 1 year follow-up according to the level of confirmation of coronary disease

Drug	After initial cardiology assessment (%)	1 year follow-up				
		Overall ($n = 3031$) (%)	Confirmed CAD ($n = 994$) (%)	Positive non-invasive ($n = 486$) (%)	Incomplete investigation ($n = 528$) (%)	Negative investigations ($n = 1023$) (%)
Antiplatelet	81	77	93	90	76	55
Aspirin	77	73	88	88	72	52
Lipid lowering	50	57	80	59	49	38
Statin	48	56	79	58	47	37
Beta-blocker	67	64	79	74	61	46
ACE inhibitor	40	42	51	46	47	28
Nitrate	59	38	43	56	48	21
Calcium antagonist	28	25	28	27	30	18
Metabolic agent	7	6	5	9	12	4
Nicorandil	2	1	2	2	0.5	0.2
Mean number of AAs	1.6 ± 0.9	1.3 ± 0.9	1.6 ± 0.8	1.7 ± 0.9	1.5 ± 0.9	0.9 ± 0.9

AA (antianginal drugs); beta-blockers, calcium antagonists, nitrate, nicorandil, or metabolic agent.

Euro Heart Survey. Eur Heart J, 2006; 27: 1298-1304



Courage Study. N Eng J Med, 2007; 356: 1503-16

The history of antischemic drugs

1785	Digoxin
1918	Quinidine
1935	Heparine
1936	Procainamide
1950	Warfarine
1963	Propanolol
1964	Furosemide
1969	Nifedipine
1986	Nitrates
1988	Ranolazine
1994	Ivabradine

European Heart Journal
doi:10.1093/eurheartj/ehl002

† Guidelines on the management of stable angina pectoris: full text‡

The Task Force on the Management of Stable Angina Pectoris of the European Society of Cardiology

Authors/Task Force Members, Kim Fox, Chairperson, London (UK)*, Maria Angeles Alonso Garcia, Madrid (Spain), Diego Ardissino, Parma (Italy), Pawel Buszman, Katowice (Poland), Paolo G. Camici, London (UK), Filippo Crea, Roma (Italy), Caroline Daly, London (UK), Guy De Backer, Ghent (Belgium), Paul Hjemdahl, Stockholm (Sweden), José Lopez-Sendon, Madrid (Spain), Jean Marco, Toulouse (France), João Morais, Leiria (Portugal), John Pepper, London (UK), Udo Sechtem, Stuttgart (Germany), Maarten Simoons, Rotterdam (The Netherlands), Kristian Thygesen, Aarhus (Denmark)

ESC Committee for Practice Guidelines (CPG), Silvia G. Priori (Chairperson) (Italy), Jean-Jacques Blanc (France), Andrzej Budaj (Poland), John Camm (UK), Veronica Dean (France), Jaap Deckers (The Netherlands), Kenneth Dickstein (Norway), John Lekakis (Greece), Keith McGregor (France), Marco Metra (Italy), João Morais (Portugal), Ady Osterspey (Germany), Juan Tamargo (Spain), José L. Zamorano (Spain)

Document Reviewers, José L. Zamorano (CPG Review Coordinator) (Spain), Felicita Andreotti (Italy), Harald Becher (UK), Rainer Dietz (Germany), Alan Fraser (UK), Huon Gray (UK), Rosa Ana Hernandez Antolin (Spain), Kurt Huber (Austria), Dimitris T. Kremastinos (Greece), Attilio Maseri (Italy), Hans-Joachim Nesser (Austria), Tomasz Pasierski (Poland), Ulrich Sigwart (Switzerland), Marco Tubaro (Italy), Michael Weis (Germany)

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Ranolazine is considered as metabolic anti-anginal drug and has been shown to be an inhibitor of the late sodium current wich is activated in case of ischaemia, leading to calcium overload of the ischaemic myocardium, decreased compliance, increased LV stiffness, and compression of capillaries. The inhibition of the late sodium current by ranolazine reverses these effects, and prevents calcium overload, and the subsequent consequences thereof.

Ranolazine has been shown to have anti-anginal efficacy. It may be used in combination therapy with hemodinamically acting agents, as their primary effect is not through reduction in heart rate or blood pressure. Ranolazine, although under intensive investigation is not yet licenced for use by the EMEA. Whether this drug influence the prognosis of patients with stable angina has not been determined.

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Guidelines of stable angina. Eur Heart J, 2006: 27: 1341-81

Ranolazine: RS 43285

ranolazine - Buscar con Google - Windows Internet Explorer

ranolazine - PubMed result - Microsoft Internet Explorer

Br. J. Pharmacol. (1988), **93**, 375–382

The effects of the novel anti-anginal compound RS 43285 on myocardial conduction in the anaesthetized dog

[1]Maxine C. Allely & B.J. Alps

Department of Pharmacology, Syntex Research Centre, Riccarton, Edinburgh, EH14 4AS

1 A pentobarbitone-anaesthetized canine model of myocardial conduction was developed to evaluate drug effects on intra-atrial (I-A), intra-ventricular (I-V) and atrioventricular (A-V) conduction parameters, both at rest and during electrical pacing of the right atrium or ventricle. Drug effects on the ability of the sino-atrial (SA) node to re-establish sinus rhythm on switching off electrical pacing were also considered. The effects of the novel anti-anginal compound RS 43285-193 ((±)-N-(2,6-dimethylphenyl)-4[2-hydroxy-3-(2-methoxyphenoxy)propyl]-1-piperazine acetamide dihydrochloride) were compared to those of the standard anti-anginal compounds nicardipine, nifedipine and verapamil.

2 In the dose range 15–7000 $\mu g\,kg^{-1}$, RS 43285 had no significant effects on I-A, I-V or A-V conduction either at rest or during electrical pacing and did not affect the re-establishment of sinus rhythm.

3 Nicardipine had no effects on conduction parameters at resting heart rate. There were no effects on I-A or I-V conduction on electrical pacing but A-V conduction was increased at 200–500 $\mu g\,kg^{-1}$ (with a 2:1 A-V conduction block in two out of six dogs); this was accompanied by a prolongation of the interval to reversion of sinus rhythm.

4 Nifedipine had no significant effects on I-A or I-V conduction but significantly prolonged A-V conduction at 1000 $\mu g\,kg^{-1}$ and this dose also increased the interval to SA node recovery.

5 Verapamil did not effect I-A or I-V conduction. However, A-V conduction was affected with a significant prolongation occurring at resting heart rate at 100–400 $\mu g\,kg^{-1}$ and a 2:1 A-V block in one

Effect of Ranolazine on HbA1c and Glucose Levels in Hyperglycemic Patients with Non-ST Elevatio - Microsoft Internet Explorer

Institution: HOSPITAL UNIV. REINA SOFIA

DiabetesCare

Effect of Ranolazine on HbA1c and Glucose Levels in Hyperglycemic Patients with Non-ST Elevation Acute Coronary Syndrome

Jeffrey W. Chisholm, PhD(jeff.chisholm@gilead.com)[1], Allison B. Goldfine, MD[2], Arvinder K. Dhalla, PhD[1], Eugene Braunwald, MD[3], David A. Morrow, MD, MPH[3], Ewa Karwatowska-Prokopczuk, MD[1] and Luiz Belardinelli, MD[4]

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[3]TIMI Study Group, Brigham and Women's Hospital and Department of Medicine, Boston, MA, USA
[4]Division of Cardiovascular Therapeutics, Gilead Sciences Inc., Foster City, CA, USA

Abstract

Objectives: We determined the relationships between glycemia at randomization, concurrent anti-diabetic therapy and change in hemoglobin A1c (HbA1c) and fasting plasma glucose (FPG) in patients with diabetes mellitus (DM) receiving standard treatment for DM and randomized to ranolazine or placebo within the MERLIN–TIMI 36 (MERLIN) study. Ranolazine is a novel first-in class drug approved for treating angina pectoris.

Myocardial Infarction

B-Type Natriuretic Peptide and the Effect of Ranolazine in Patients With Non–ST-Segment Elevation Acute Coronary Syndromes

Observations From the MERLIN–TIMI 36 (Metabolic Efficiency With Ranolazine for Less Ischemia in Non–ST Elevation Acute Coronary–Thrombolysis In Myocardial Infarction 36) Trial

David A. Morrow, MD, MPH,*† Benjamin M. Scirica, MD, MPH,*† Marc S. Sabatine, MD, MPH,*† James A. de Lemos, MD,§ Sabina A. Murphy, MPH,* Pete Jarolim, MD, PhD,‖ Pierre Theroux, MD,‖ Christophe Bode, MD,¶ Eugene Braunwald, MD*†

Boston, Massachusetts; Dallas, Texas; Montreal, Quebec, Canada; and Freiburg, Germany

Objectives — We designed a prospective evaluation of the interaction between B-type natriuretic peptide (BNP) and the effect of ranolazine in patients with acute coronary syndromes (ACS) as part of a randomized, blinded, placebo-controlled trial.

Background — Ranolazine is believed to exert anti-ischemic effects by reducing myocardial sodium and calcium overload and consequently ventricular wall stress. BNP increases in response to increased wall stress and is a strong risk indicator in ACS.

Methods — We measured plasma BNP in all available baseline samples (n = 4,643) among patients with non-ST-segment elevation ACS randomized to ranolazine or placebo in the MERLIN-TIMI 36 (Metabolic Efficiency With Ranolazine for Less Ischemia in Non-ST Elevation Acute Coronary–Thrombolysis In Myocardial Infarction 36) trial and followed them for a mean of 343 days. The primary end point was a composite of cardiovascular death, myocardial infarction, and recurrent ischemia. BNP elevation was defined as >80 pg/ml.

Results — Patients with elevated BNP (n = 1,935) were at significantly higher risk of the primary trial end point (26.4% vs. 20.8%, p < 0.0001), cardiovascular death (8.0% vs. 2.8%, p < 0.001), and myocardial infarction (10.6% vs. 6.8%, p < 0.001) at 1 year. In patients with BNP >80 pg/ml, ranolazine reduced the primary end point (hazard ratio [HR]: 0.79, 95% confidence interval [CI]: 0.66 to 0.94, p = 0.009). The effect of ranolazine in patients with BNP >80 pg/ml was directionally similar for recurrent ischemia (HR: 0.79, 95% CI: 0.62 to 0.98, p = 0.04) and cardiovascular death or myocardial infarction (HR: 0.83, 95% CI: 0.66 to 1.05, p = 0.12). There was no detectable effect in those with low BNP (p interaction value = 0.05).

Conclusions — Our findings indicate that ranolazine may have enhanced efficacy in high-risk patients with ACS identified by increased BNP. The interaction of biomarkers of hemodynamic stress and the effects of ranolazine warrants additional investigation. (Metabolic Efficiency With Ranolazine for Less Ischemia in Non–ST Elevation Acute Coronary Syndromes; NCT00099788) (J Am Coll Cardiol 2010;55:1189–96) © 2010 by the American College of Cardiology Foundation

Indian PACING and ELECTROPHYSIOLOGY Journal www.ipej.org

Original Article

The Use Of Oral Ranolazine To Convert New O Paroxysmal Atrial Fibrillation: A Review Of Experienc With Implications For Possible "Pill In The Pocket Approach To Atrial Fibrillation

David K Murdock MD, Mary Kersten RN, Jeff Kaliebe MT, CCRC, German Larrain MD

The Aspirus Heart and Vascular Institute, Cardiovascular Associates of Northern Wisconsin ar The CaRE Foundation, Wausau Wisconsin USA

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Ranolazine—Treatment of Ventricular Tachycardia and Symptomatic Ventricular Premature Beats in Ischemic Cardiomyopathy

SUDIP NANDA, M.D., VADIM LEVIN, M.D., MATTHEW W. MARTINEZ, M.D., and RONALD FREUDENBERGER, M.D.

From the Lehigh Valley Hospital, Cedar Crest, Allentown, Pennsylvania

Premature ventricular complexes (PVCs) are a frequent occurrence in the presence of ischemic heart disease. A very high PVC load can be symptomatic or occasionally result in a cardiomyopathy (CMP). Treatment options include pharmacologic agents and radiofrequency ablation (RFA). RFA has been successful in treating PVCs in symptomatic patients or in the presence of unexplained CMP. Ranolazine is a piperazine derivative used for treating chronic stable angina. It also has antiarrhythmic properties. We report a patient with ischemic CMP, symptomatic PVCs, and monomorphic ventricular tachycardia (VT) despite attempts to control symptoms with two antiarrhythmic drugs. Initiation of ranolazine led to marked reduction in PVCs along with control of VT and symptoms. (PACE 2010; 1–2)

Coronary Heart Disease

Clinical Features and Outcomes of Women With Unstable Ischemic Heart Disease

Observations From Metabolic Efficiency With Ranolazine for Less Ischemia in Non–ST-Elevation Acute Coronary Syndromes–Thrombolysis in Myocardial Infarction 36 (MERLIN-TIMI 36)

Jessica L. Mega, MD, MPH; Judith S. Hochman, MD; Benjamin M. Scirica, MD, MPH; Sabina A. Murphy, MPH; Sarah Sloan, MA, MS; Carolyn H. McCabe, BS; Piera Merlini, MD; David A. Morrow, MD, MPH

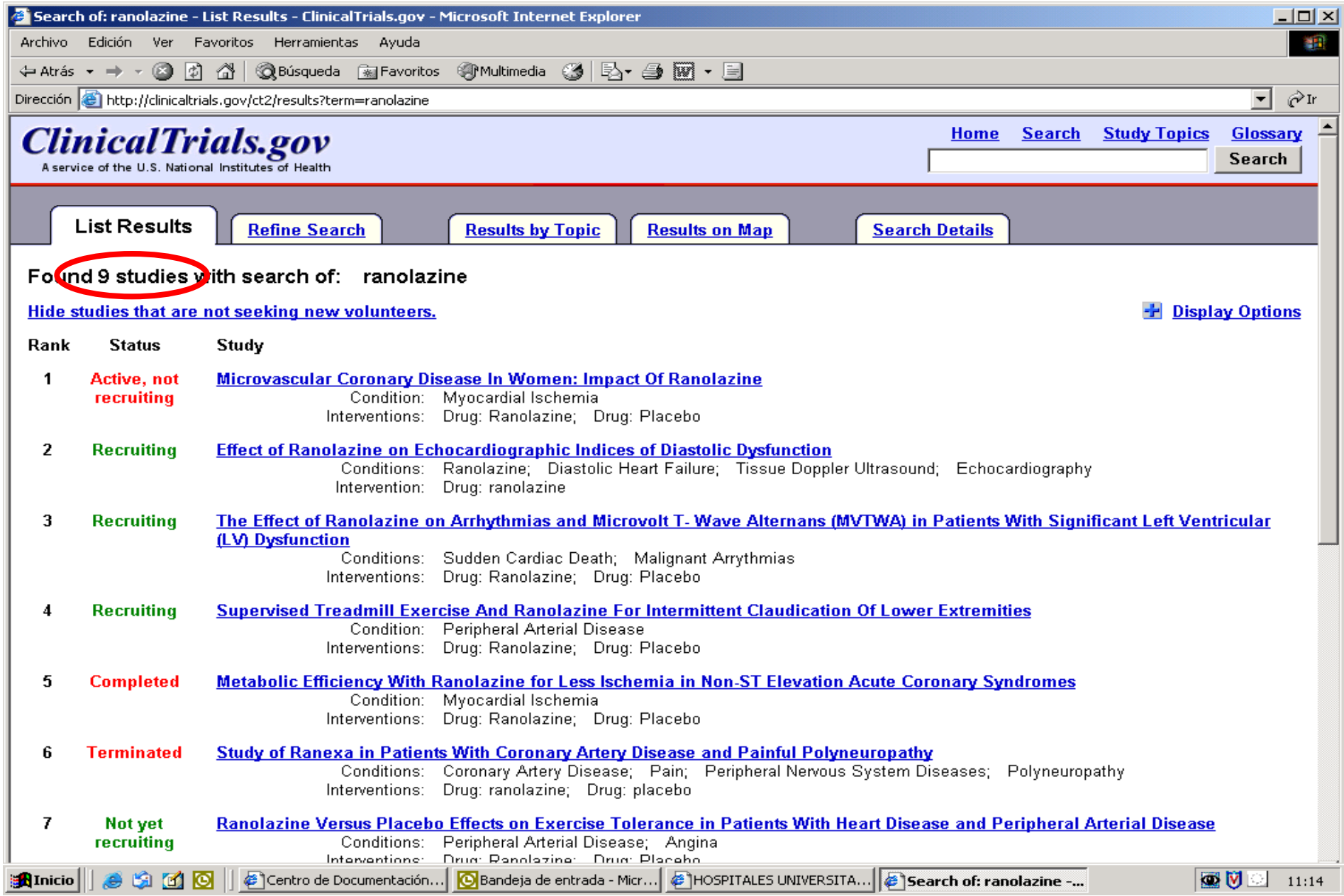
Background—The pathobiological basis of ischemic heart disease and thus the manifestations and response to therapy can differ between women and men. In prior studies, sex-based treatment differences have been observed with the antiischemic ranolazine, with a possibly diminished effect in women.

Methods and Results—We conducted a prospectively planned analysis of the clinical, biomarker, angiographic, and continuous ECG features and 1-year outcomes of women with unstable ischemic heart disease randomized to ranolazine or placebo in Metabolic Efficiency With Ranolazine for Less Ischemia in Non–ST-Elevation Acute Coronary Syndromes–Thrombolysis in Myocardial Infarction 36 (MERLIN-TIMI 36). Compared with men (n=4269), women (n=2291) were older with more risk factors ($P<0.001$). On presentation, women were less likely than men to have significant epicardial coronary artery disease (no stenosis ≥50% on angiography, 19.4% versus 8.6%; $P<0.001$) or elevated troponin (57.1% versus 68.9%; $P<0.001$). Yet, women were more likely to have an elevated B-type natriuretic peptide (47.0% versus 40.2%; $P<0.001$), worse median angina frequency scores (80 versus 100; $P<0.001$), and an ischemic episode on continuous ECG administered during the first 7 days (22.5% versus 19.3%; $P=0.0025$). Women and men were at similar adjusted risk for the primary end point of cardiovascular death, myocardial infarction, or recurrent ischemia (adjusted hazard ratio, 1.11; 95% confidence interval, 0.96 to 1.29; $P=0.15$). Ranolazine was associated with a significant reduction in recurrent ischemia in women (13.0% versus 18.2%; hazard ratio, 0.71; 95% confidence interval, 0.57 to 0.88; $P=0.002$).

Conclusions—Women with a clinical syndrome consistent with unstable ischemic heart disease, despite having less obstructive coronary artery disease, were more likely than men to report anginal episodes and had more recorded ischemic periods on continuous ECG. In this setting, ranolazine may be a particularly useful antiischemic agent in women.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00099788.

(*Circulation*. 2010;121:1809-1817.)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Display Options
Rank Status Study
1 Active, not recruiting Microvascular Coronary Disease In Women: Impact Of Ranolazine
Condition: Myocardial Ischemia
Interventions: Drug: Ranolazine; Drug: Placebo
2 Recruiting Effect of Ranolazine on Echocardiographic Indices of Diastolic Dysfunction
Conditions: Ranolazine; Diastolic Heart Failure; Tissue Doppler Ultrasound; Echocardiography
Intervention: Drug: ranolazine
3 Recruiting The Effect of Ranolazine on Arrhythmias and Microvolt T- Wave Alternans (MVTWA) in Patients With Significant Left Ventricular (LV) Dysfunction
Conditions: Sudden Cardiac Death; Malignant Arrythmias
Interventions: Drug: Ranolazine; Drug: Placebo
4 Recruiting Supervised Treadmill Exercise And Ranolazine For Intermittent Claudication Of Lower Extremities
Condition: Peripheral Arterial Disease
Interventions: Drug: Ranolazine; Drug: Placebo
5 Completed Metabolic Efficiency With Ranolazine for Less Ischemia in Non-ST Elevation Acute Coronary Syndromes
Condition: Myocardial Ischemia
Interventions: Drug: Ranolazine; Drug: Placebo
6 Terminated Study of Ranexa in Patients With Coronary Artery Disease and Painful Polyneuropathy
Conditions: Coronary Artery Disease; Pain; Peripheral Nervous System Diseases; Polyneuropathy
Interventions: Drug: ranolazine; Drug: placebo
7 Not yet recruiting Ranolazine Versus Placebo Effects on Exercise Tolerance in Patients With Heart Disease and Peripheral Arterial Disease
Conditions: Peripheral Arterial Disease; Angina
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SYMPOSIUM

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Ranolazina: un nuovo farmaco per migliorare la qualità della vita nei pazienti con angina stabile sintomatica
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Conclusioni
F. Fedele (*Roma*)

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