XXX Congreso Sociedad Española Medicina Interna

Nuevas oportunidades para nuestros pacientes

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Arritmias y Electrofisiología

Nuevas oportunidades

- Nuevos Fármacos Antiarrítmicos
- Nuevos Fármacos Anticoagulantes
- Ablación con catéter

FAA

Fármacos Antiarrítmicos

Azimilide

Azimilide
Estudio A-COMET-II

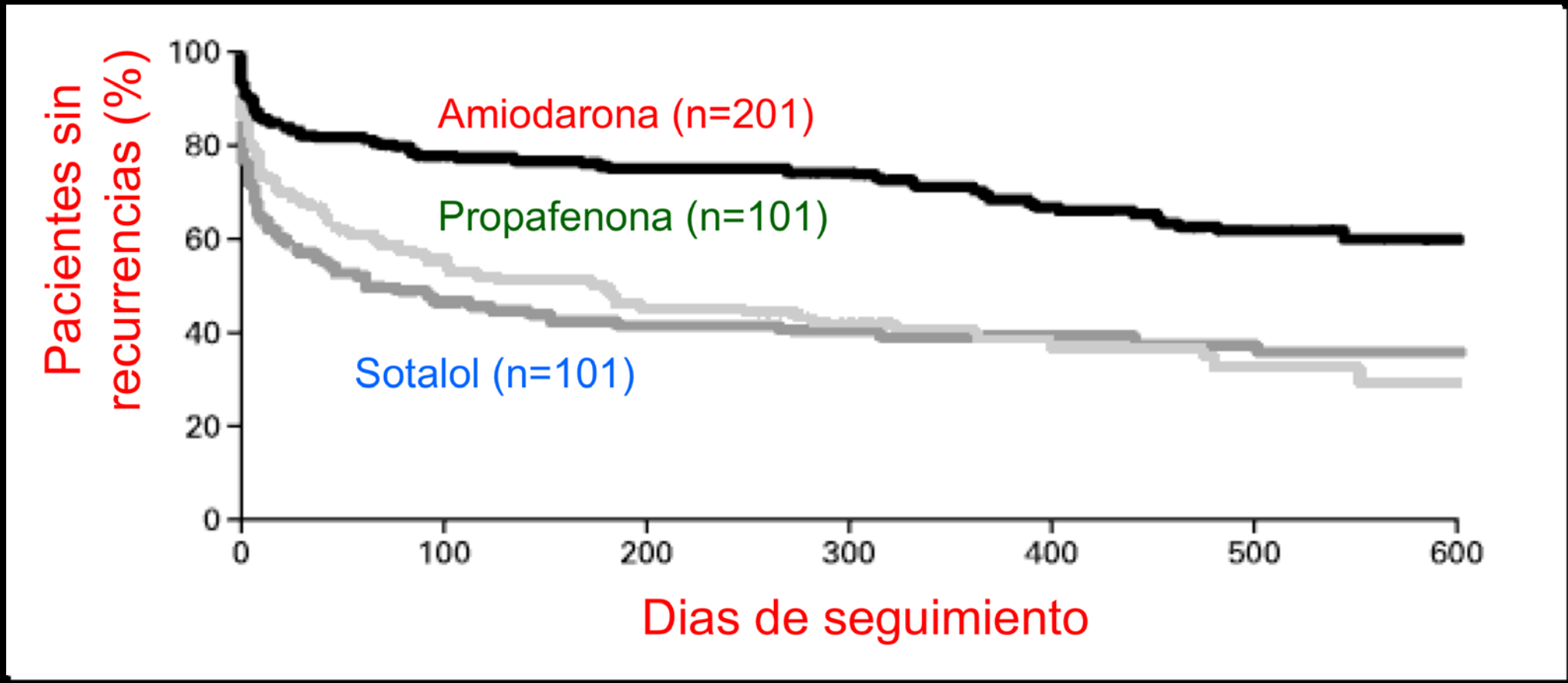
- FA persistente y CVE 658 pts
- Azimilide vs Sotalol vs Placebo
- No FA en 26 semanas:
  - 33% sotalol (P<0.01)
  - 19% azimilide
  - 15% placebo
- Menor efecto que Sotalol
  Mayor QTL/TdP que Sotalol

Lombardi et al. *Eur Heart J 2006*

Fármacos Antiarrítmicos

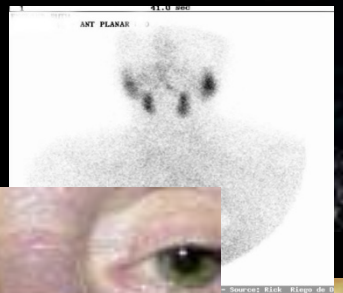
Dronedarona

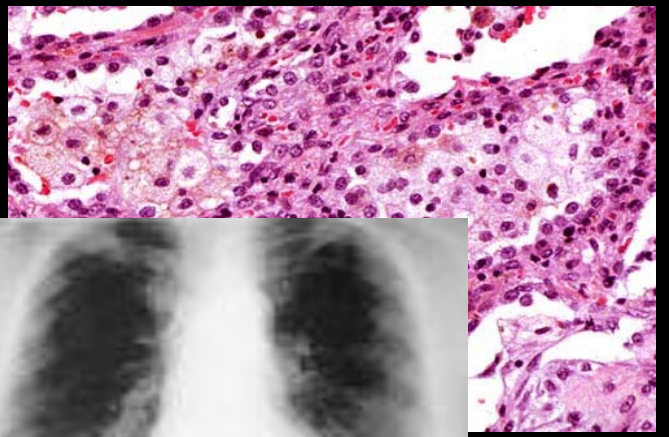
The Canadian Trial of AF

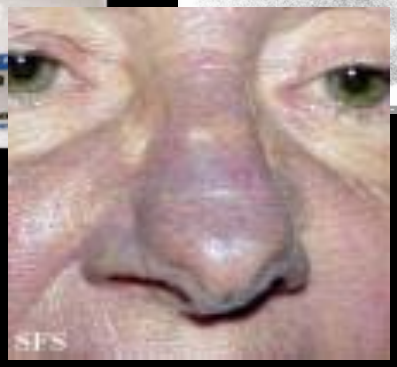


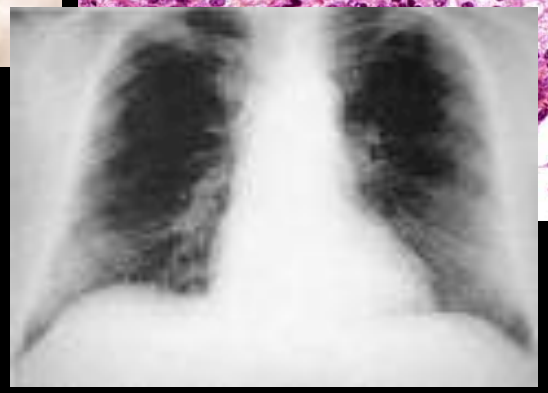
Roy D et al. NEJM 2000;342:913

Efectos adversos amiodarona



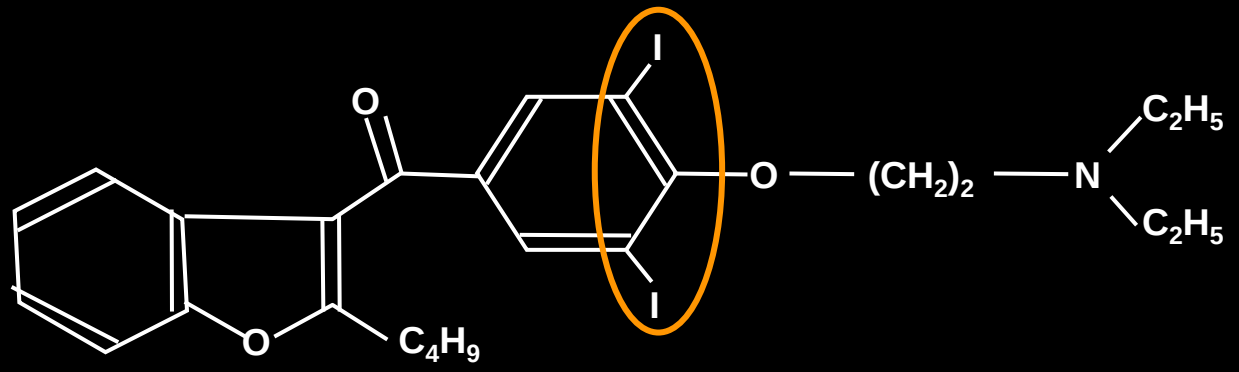




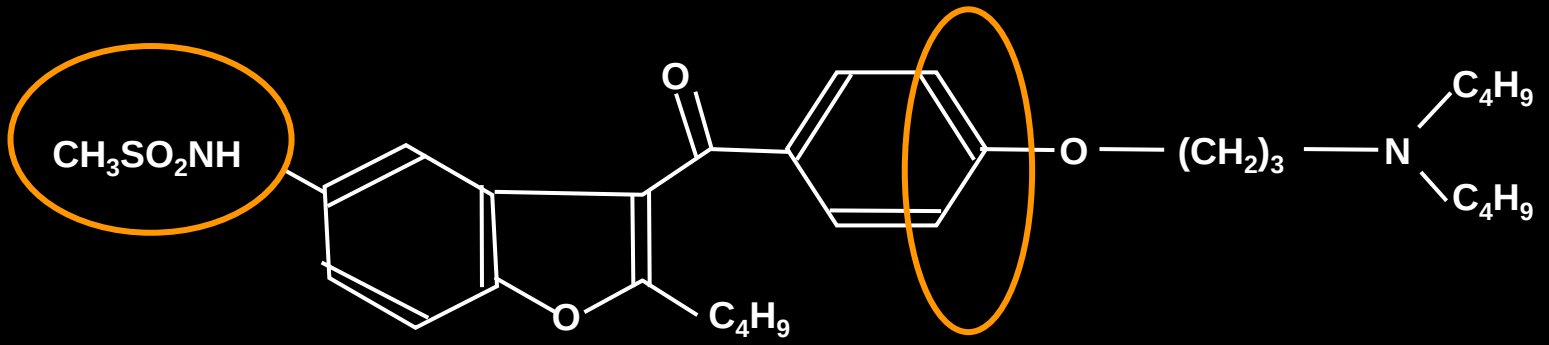


10-23%

Dronedarona



Amiodarona



Dronedarona

Sun et al. Circulation 1999

Farmacología

- **Buena absorción VO**

  ~ 15% bioavailabilidad

- **Alta metabolización (CYP3A4)**

  Excreción digestiva (biliar)

  t_{max} ~ 3–6 hs

  $t_{1/2}$: 27–31 hs

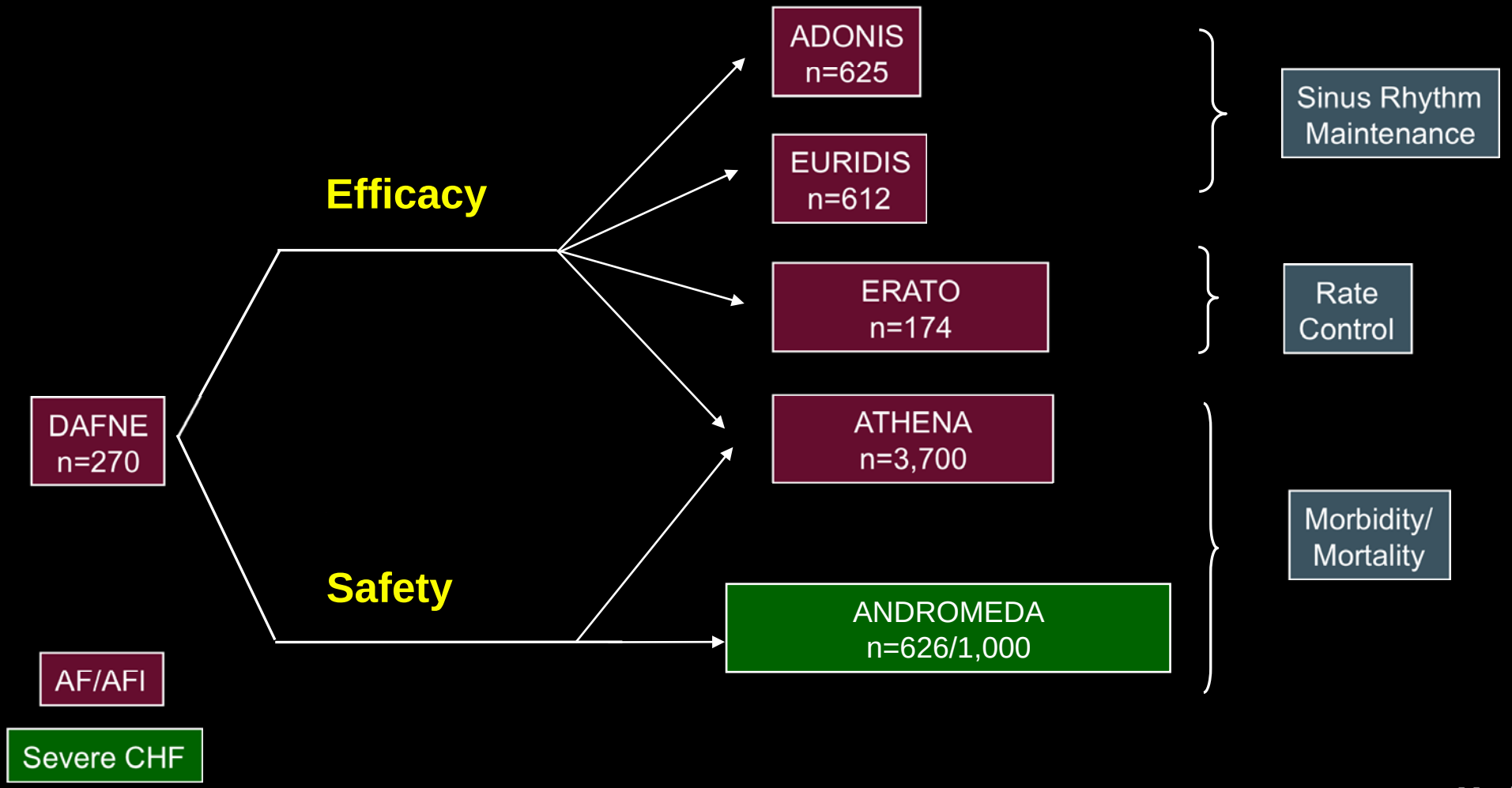
- **No influencia sexo o edad**

Dronedarona no induce *Torsade de Pointes*

	Dose (µg/kg/min)	PVCs (%)	VT (%)	TdeP (%)	QTc (%)
Vehicle	PEG_{400} 75%	29	0	0	+4
Dofetilide	10	100*	54*	45*	+37*
Amiodarone	100–300	0	0	0	+1 to +12
Dronedarone	30–100	0	0	0	-3 to -7

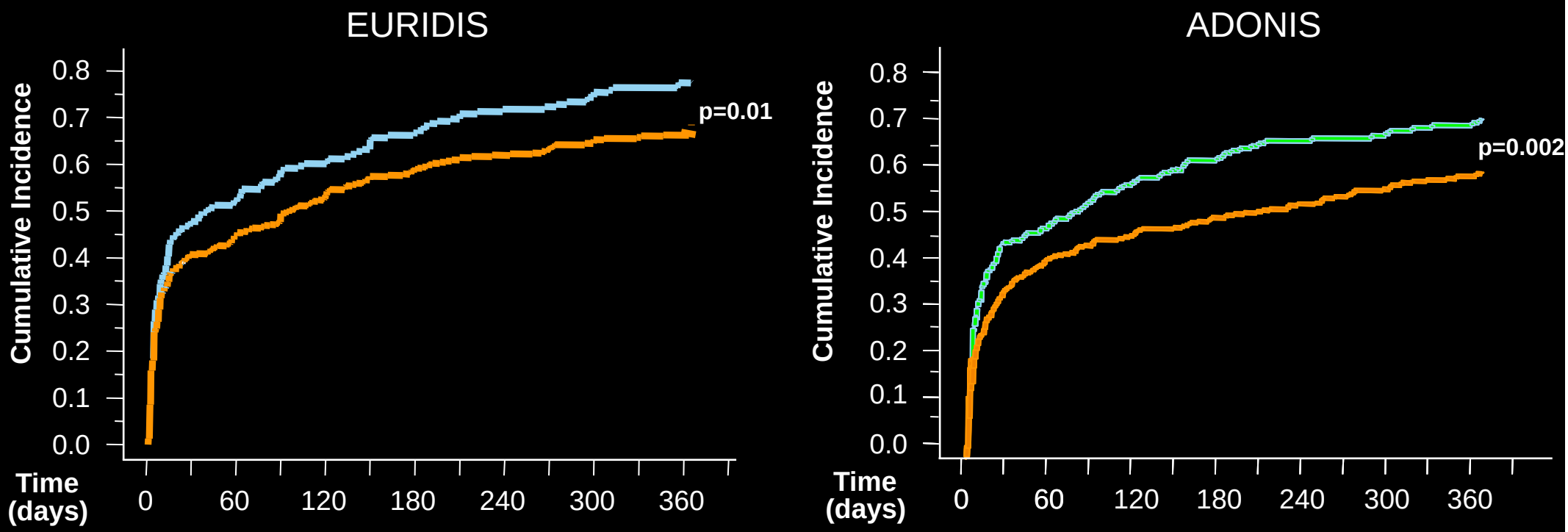
Serre *et al. Fund Clin Pharmacol* 2001

Estudios clínicos Dronedarona



Estudios EURIDIS y ADONIS

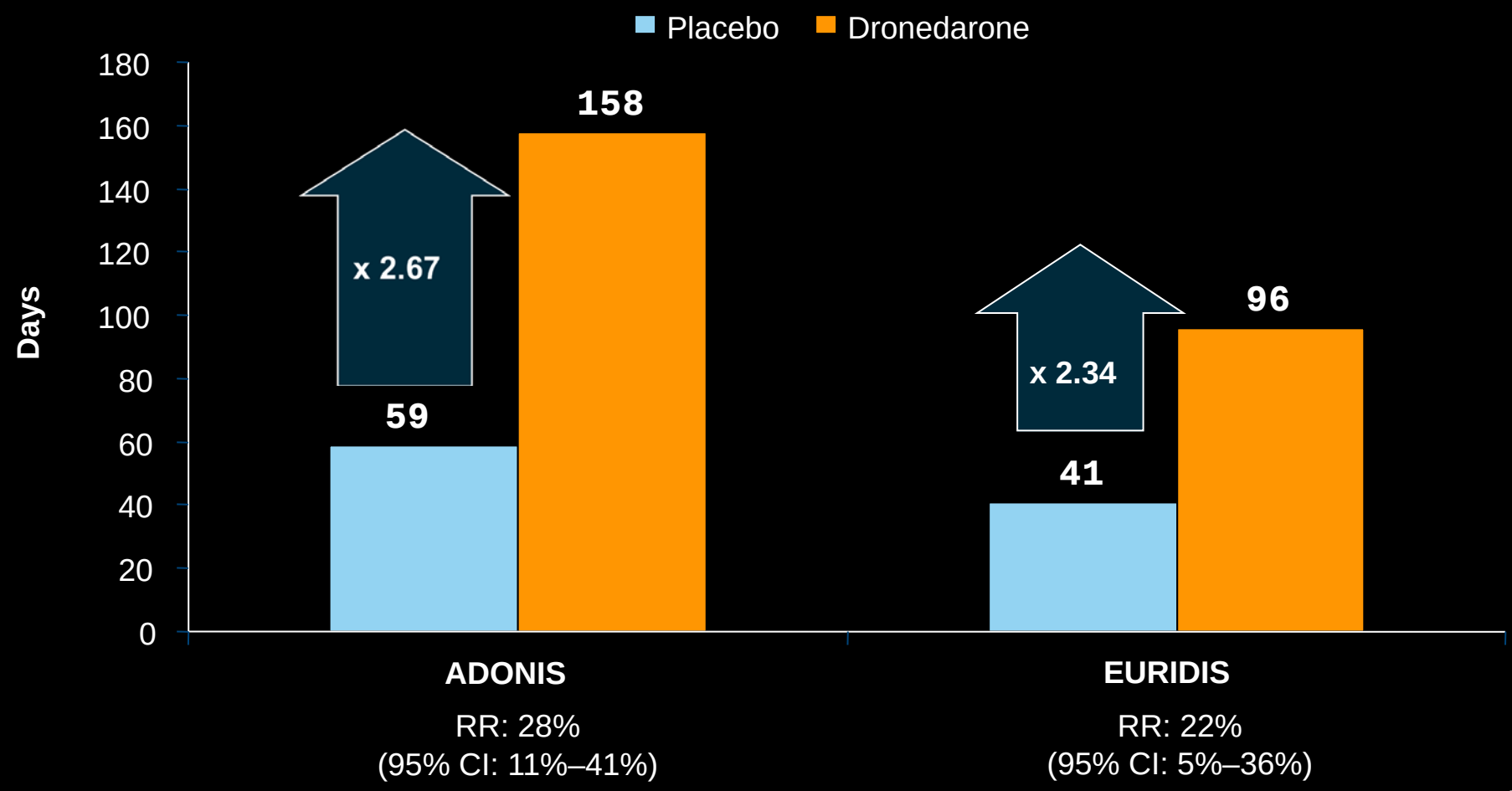
Recurrencia FA



Singh *et al.* N Engl J Med 2007

Estudios EURIDIS y ADONIS

Tiempo a la 1ª recurrencia FA



Merino 14

ANDROMEDA

ANtiarrhythmic trial with DRONedarone in Moderate to severe CHF Evaluation morbidity DecreAse

Estudio ANDROMEDA

- **N = 627**
  FE <35% y NYHA III-IV *(RS el 75%)*
  Ingreso por ICC <7 días

- **Dronedarona vs Placebo**

- **Resultados:**
  - **Objetivo 1ª: Muerte o Hospitaliz CV (P=0,12)**
  - **Mortalidad:**
    - **Dronedarone 25**
    - **Placebo 12**

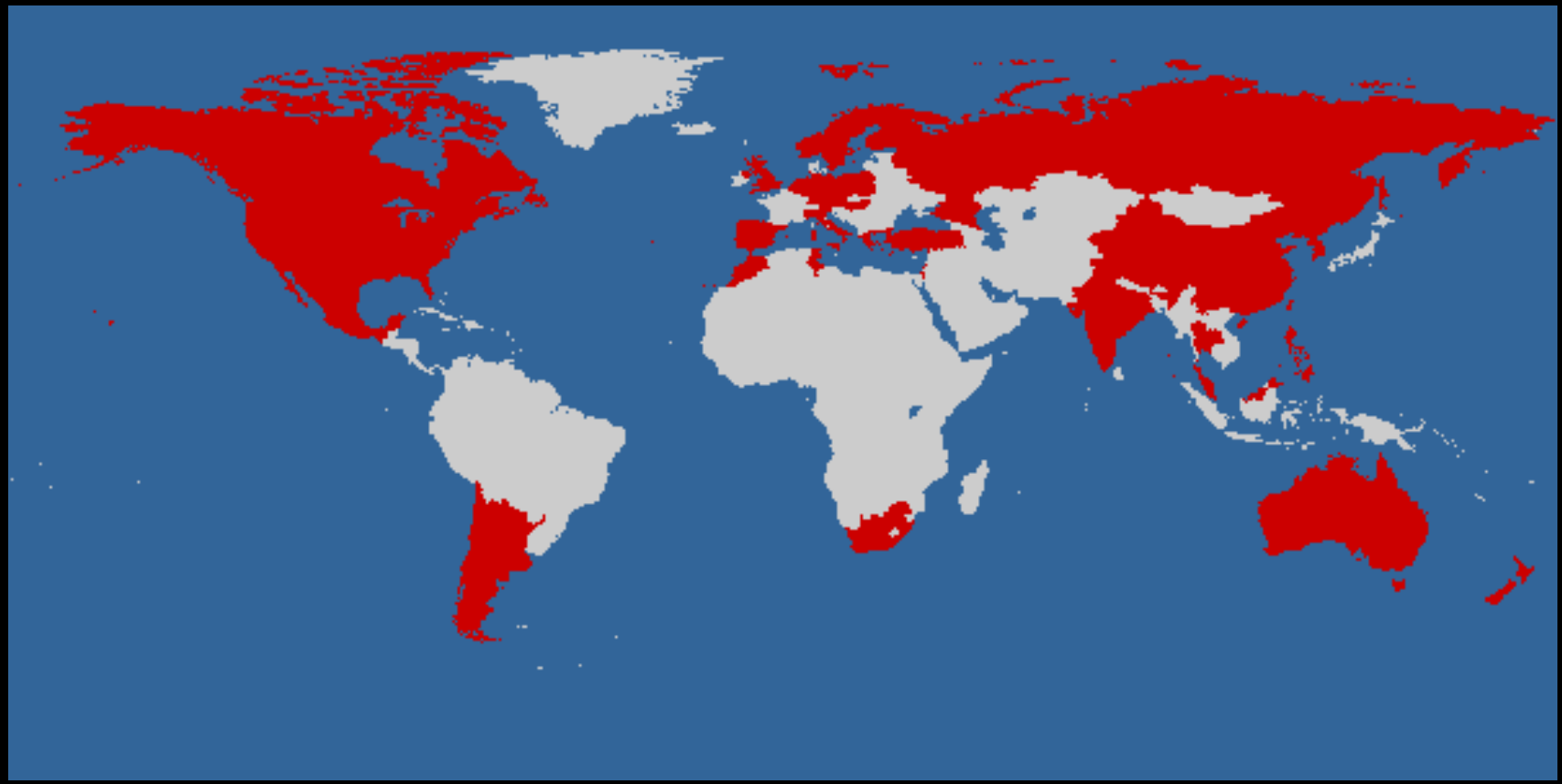
    P=0,03

    → **Acumulado en retiro IECAs**

Estudio ATHENA

Estudio ATHENA

- N = 4628 pts
- 551 centros 37 países



Estudio ATHENA

- **Dronedarona vs Placebo**
- **FA persistente +**
  - **>75 años**
  - **>70 años + 1FR** (ACV, HTA, DBM, FEVI ≤40%, AI ≥50 mm)
- **Objetivo:**
  Mortalidad y/o hospitalización CV a 1 año

The NEW ENGLAND JOURNAL of MEDICINE

N ENGL J MED 360;7 NEJM.ORG FEBRUARY 12, 2009

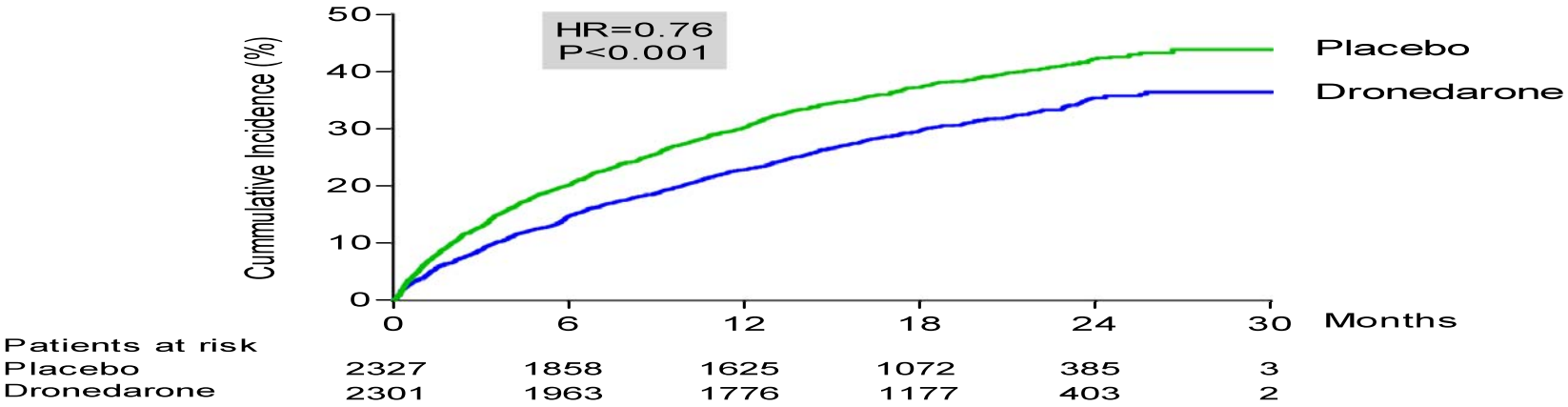
ORIGINAL ARTICLE

Effect of Dronedarone on Cardiovascular Events in Atrial Fibrillation

Stefan H. Hohnloser, M.D., Harry J.G.M. Crijns, M.D., Martin van Eickels, M.D., Christophe Gaudin, M.D., Richard L. Page, M.D., Christian Torp-Pedersen, M.D., and Stuart J. Connolly, M.D., for the ATHENA Investigators*

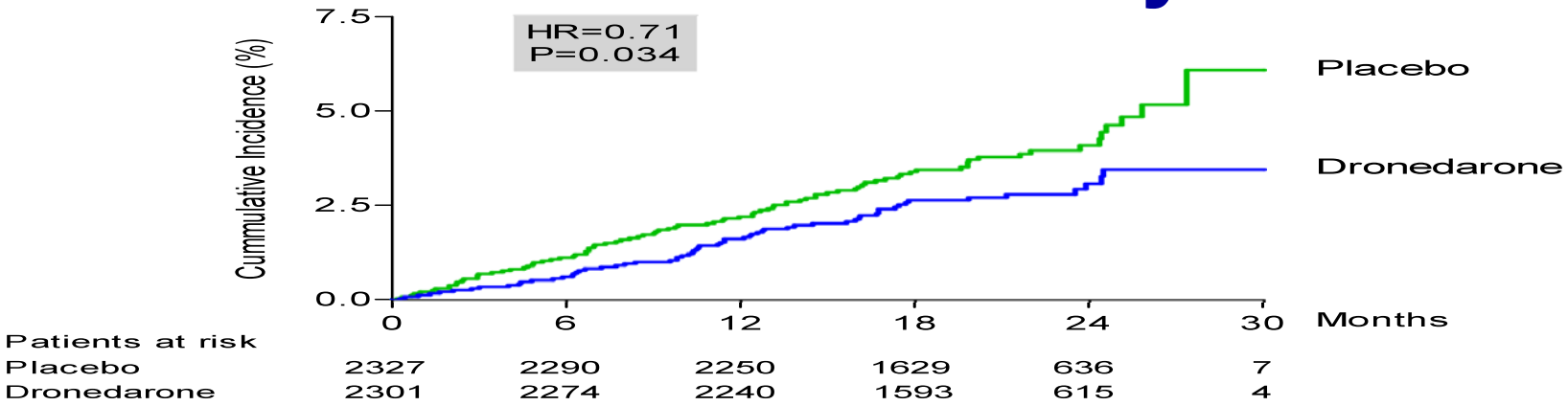
ATHENA Trial

Primary Outcome



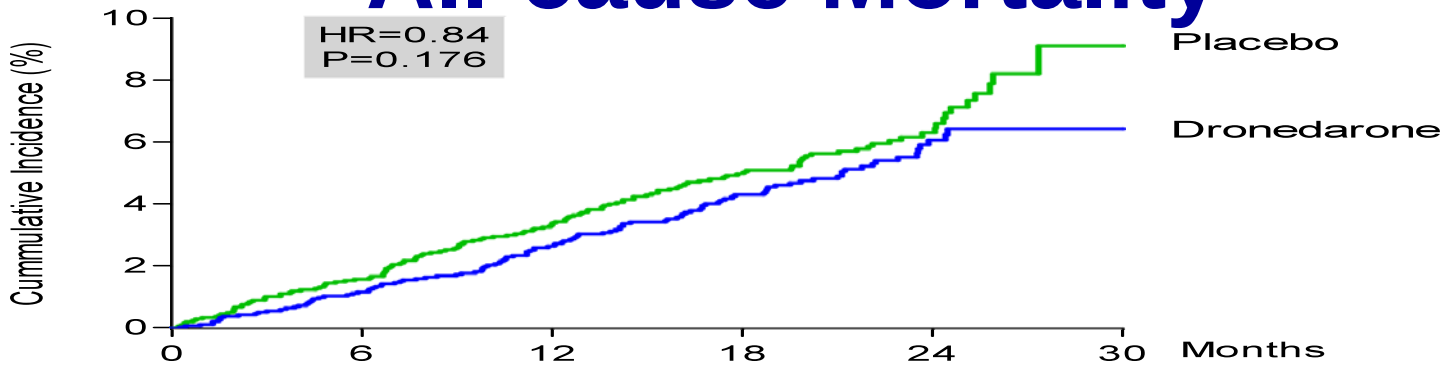
ATHENA Trial

CV Mortality



ATHENA Trial

All-cause Mortality

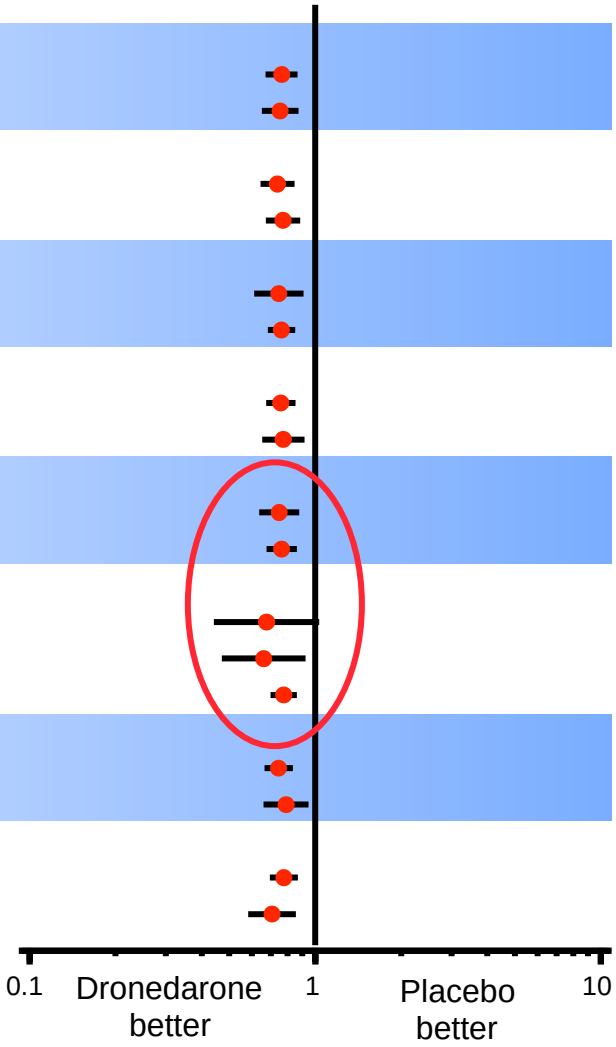


Patients at risk						
Placebo	2327	2290	2250	1629	636	7
Dronedarone	2301	2274	2240	1593	615	4

ATHENA Trial

Hazard Ratios for Primary Outcome in Important Clinical Subgroups

Characteristic	N	HR [95% CI]	P-value
Age (years)			
<75	2703	0.76 [0.67;0.87]	
>=75	1925	0.75 [0.65;0.87]	0.93
Gender			
Male	2459	0.74 [0.64;0.85]	
Female	2169	0.77 [0.67;0.89]	0.65
Presence of AF/AFL			
Yes	1155	0.74 [0.61;0.91]	
No	3473	0.76 [0.68;0.85]	0.85
Structural Heart Disease			
Yes	2732	0.76 [0.67;0.85]	
No	1853	0.77 [0.65;0.92]	0.85
Congestive Heart Failure			
Yes	1365	0.75 [0.64;0.88]	
No	3263	0.76 [0.68;0.86]	0.83
LVEF (%)			
<35	179	0.68 [0.44;1.03]	
[35-45[	361	0.66 [0.47;0.92]	
>=45	4004	0.78 [0.70;0.86]	0.30
ACE/ARB			
Yes	3216	0.74 [0.66;0.83]	
No	1412	0.79 [0.66;0.95]	0.59
Beta Blocking Agents			
Yes	3269	0.78 [0.69;0.87]	
No	1359	0.71 [0.58;0.86]	0.41



La pregunta

¿Dronedarona o Amiodarona?

Estudio DIONYSOS

DIONYSOS

504 pts

Dronedarona	Amiodarona
400 mg bid	**200 mg/d**

7 meses

Objetivos:

Recurrencia FA o discontinuación por 2^{arios}

Resultados

	Drone	Amio	
Recurrencia FA	36%	24%	
Adversos	83 pts	107 pts	P=NS
Adversos sin G-I	61 pts	99 pts	P=0.002

Dronedarona

Indicaciones:

- **Control ritmo FA (sobretodo si FR: HTA, etc)**
- **Control FC**

Contraindicaciones:

- **ICC grave descompensada (FE<35%)**

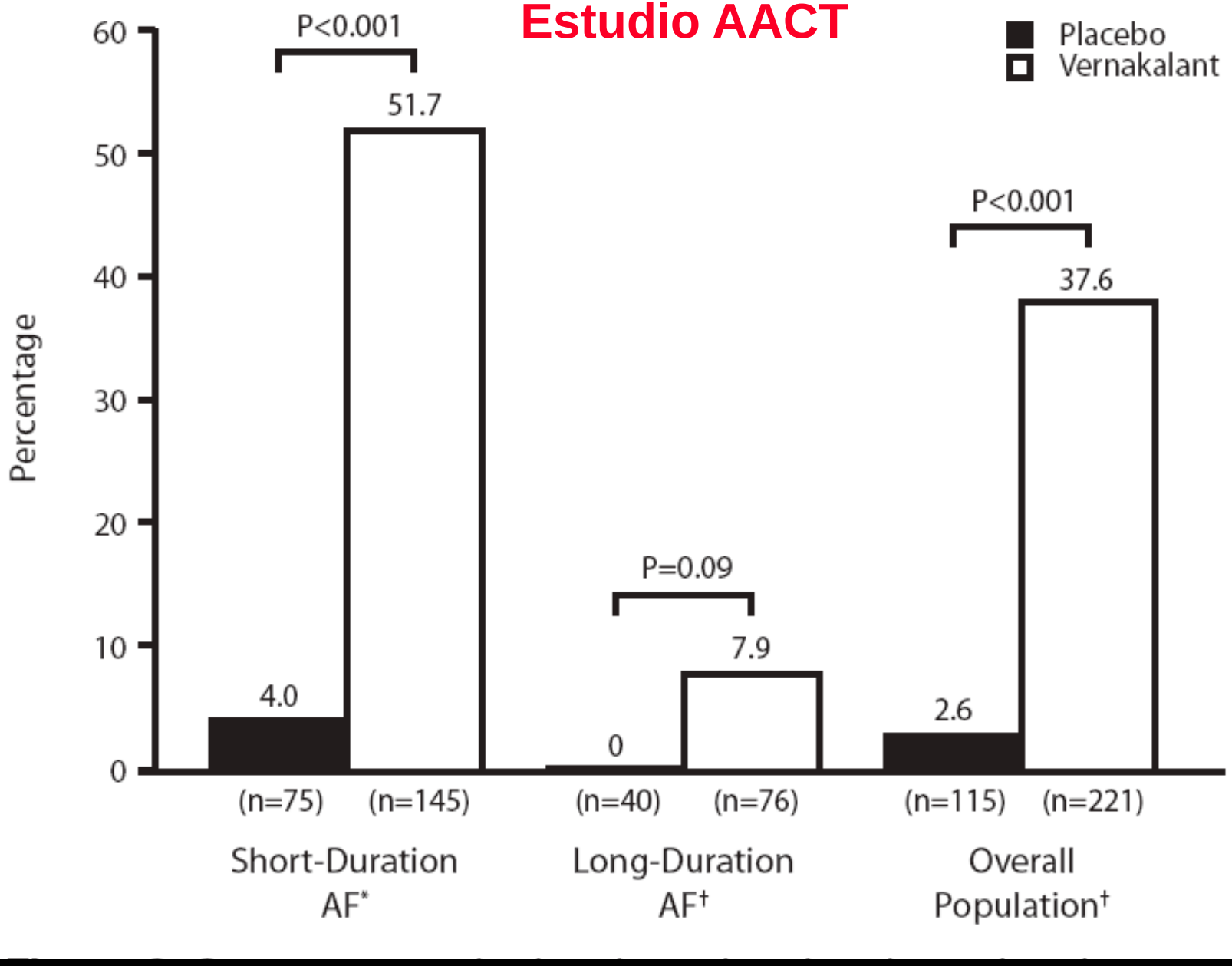
Fármacos Antiarrítmicos

“Atrio-selectivos”

Vernakalant

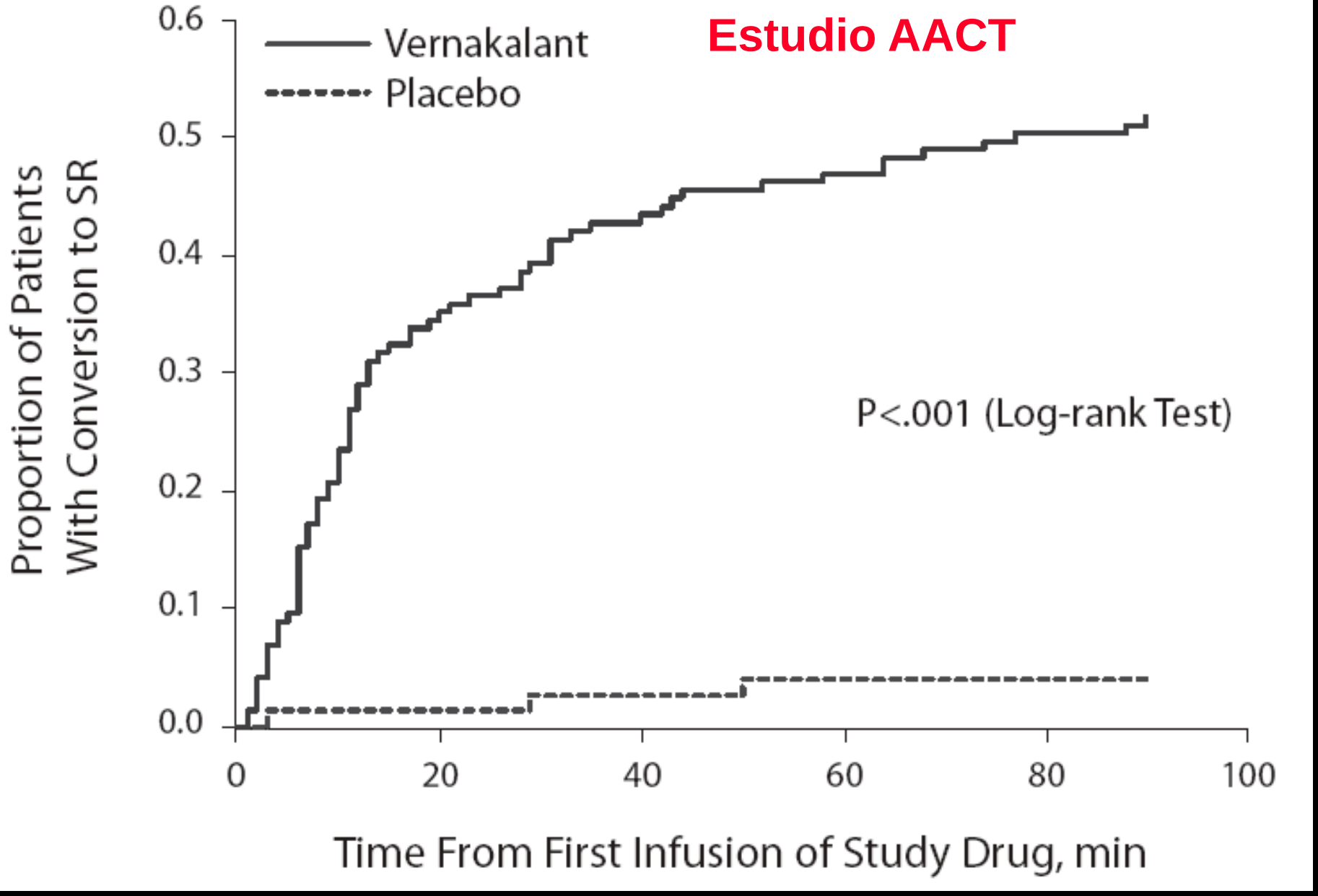
- RSD1235
- FAA tipo III
- Selectivo miocárdio auricular (IK_{UR})
- V.O. y I.V.

Estudio AACT



Roy et al. *Circulation 2008*

Estudio AACT



Roy et al. *Circulation 2008*

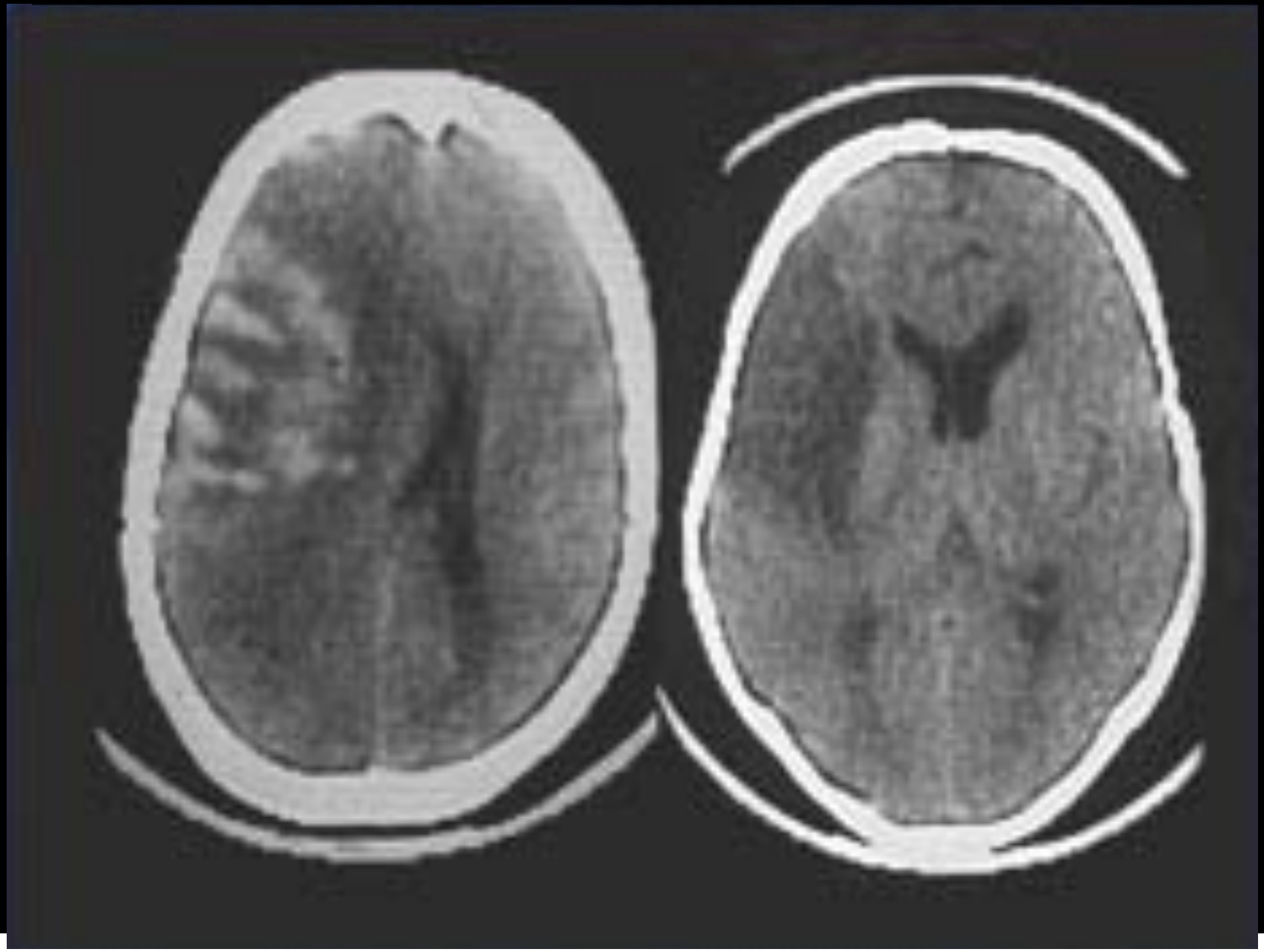
Fármacos Antiarrítmicos

Otros

- **Moduladores Gap Junctions**
- **Antagonistas 5-ht4**

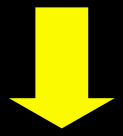
Antitrombóticos

Infarto cerebral

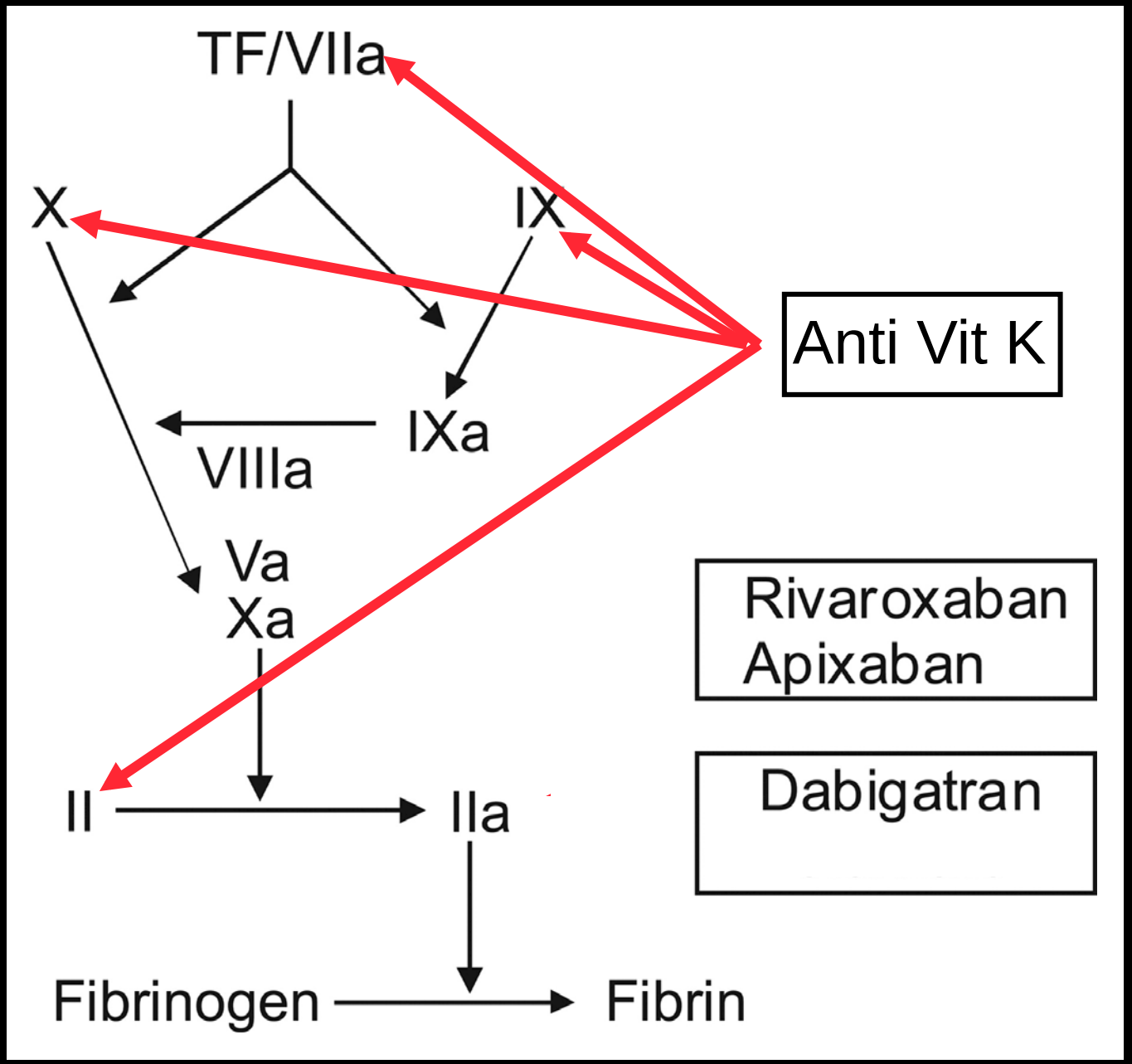


Limitaciones Antagonistas Vit K

- Ventana terapéutica estrecha
- Inicio y terminación efecto gradual
- Metabolismo afectado por:
  - Dieta
  - Fármacos
  - Polimorfismos genéticos



- Necesidad de monitorización
- Riesgo hemorrágico


TF/VIIa
X
IX
Anti Vit K
IXa
VIIIa
Va
Xa
Rivaroxaban
Apixaban
Dabigatran
II
IIa
Fibrinogen
Fibrin

Nuevos Anticoag

● Ximelagatran	SPORTIF III y V	II
Dabigatran	RE-LY	
● Edoxaban	ENGAGE-AF (TIMI 48)	Xa
Ribaroxaban	ROCKET-AF	
Apixaban	ARISTOLE	
	AVERROES	
● Idraparinux	AMADEUS	
	BOREALIS (bioetilinato)	

RE-LY trial

The NEW ENGLAND JOURNAL of MEDICINE

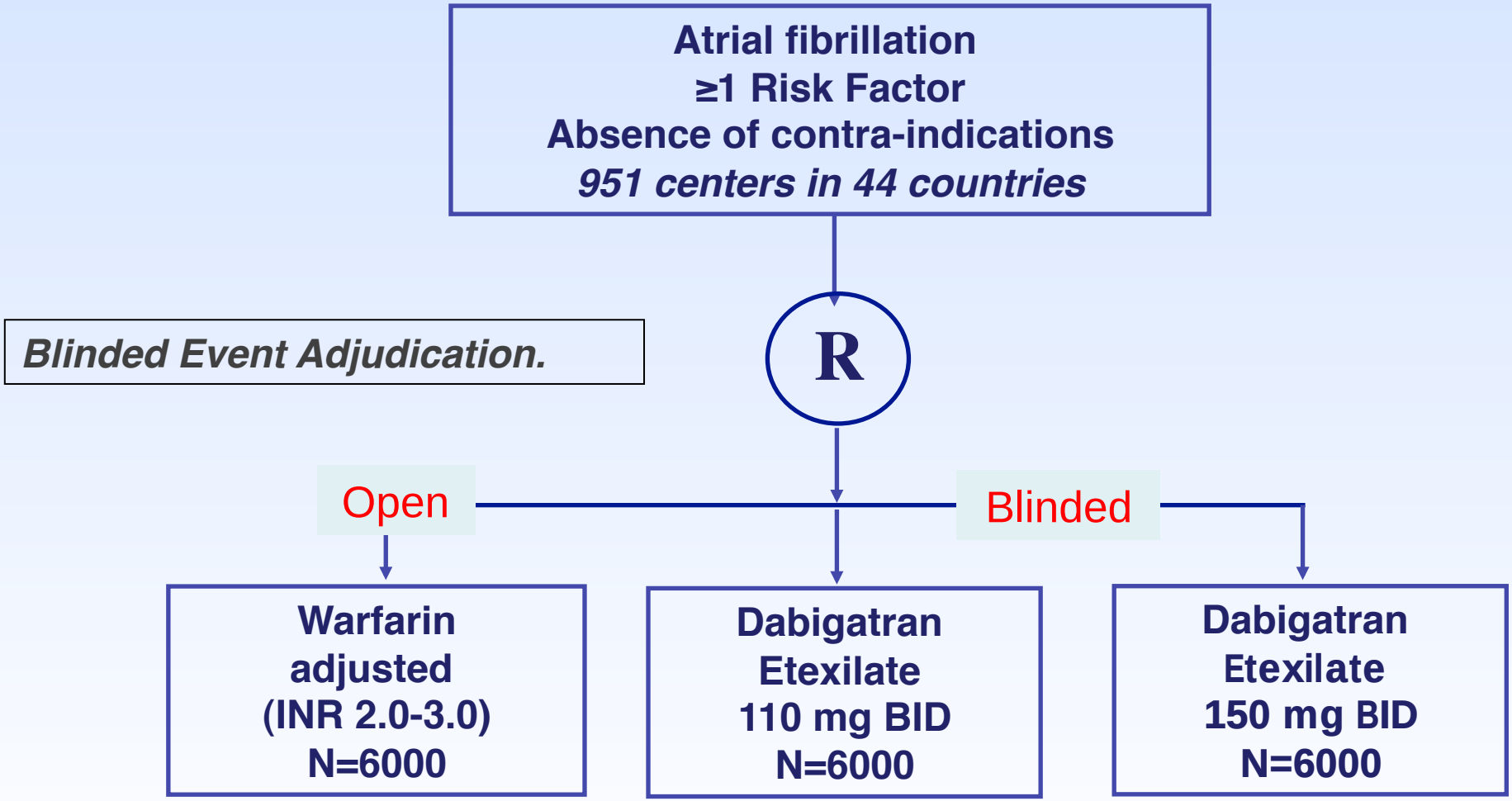
Aug 2009

Dabigatran versus Warfarin in Patients with Atrial Fibrillation

Stuart J. Connolly, M.D., Michael D. Ezekowitz, M.B., Ch.B., D.Phil., Salim Yusuf, F.R.C.P.C., D.Phil., John Eikelboom, M.D., Jonas Oldgren, M.D., Ph.D., Amit Parekh, M.D., Janice Pogue, M.Sc., Paul A. Reilly, Ph.D., Ellison Themeles, B.A., Jeanne Varrone, M.D., Susan Wang, Ph.D., Marco Alings, M.D., Ph.D., Denis Xavier, M.D., Jun Zhu, M.D., Rafael Diaz, M.D., Basil S. Lewis, M.D., Harald Darius, M.D., Hans-Christoph Diener, M.D., Ph.D., Campbell D. Joyner, M.D., Lars Wallentin, M.D., Ph.D., and the RE-LY Steering Committee and Investigators*

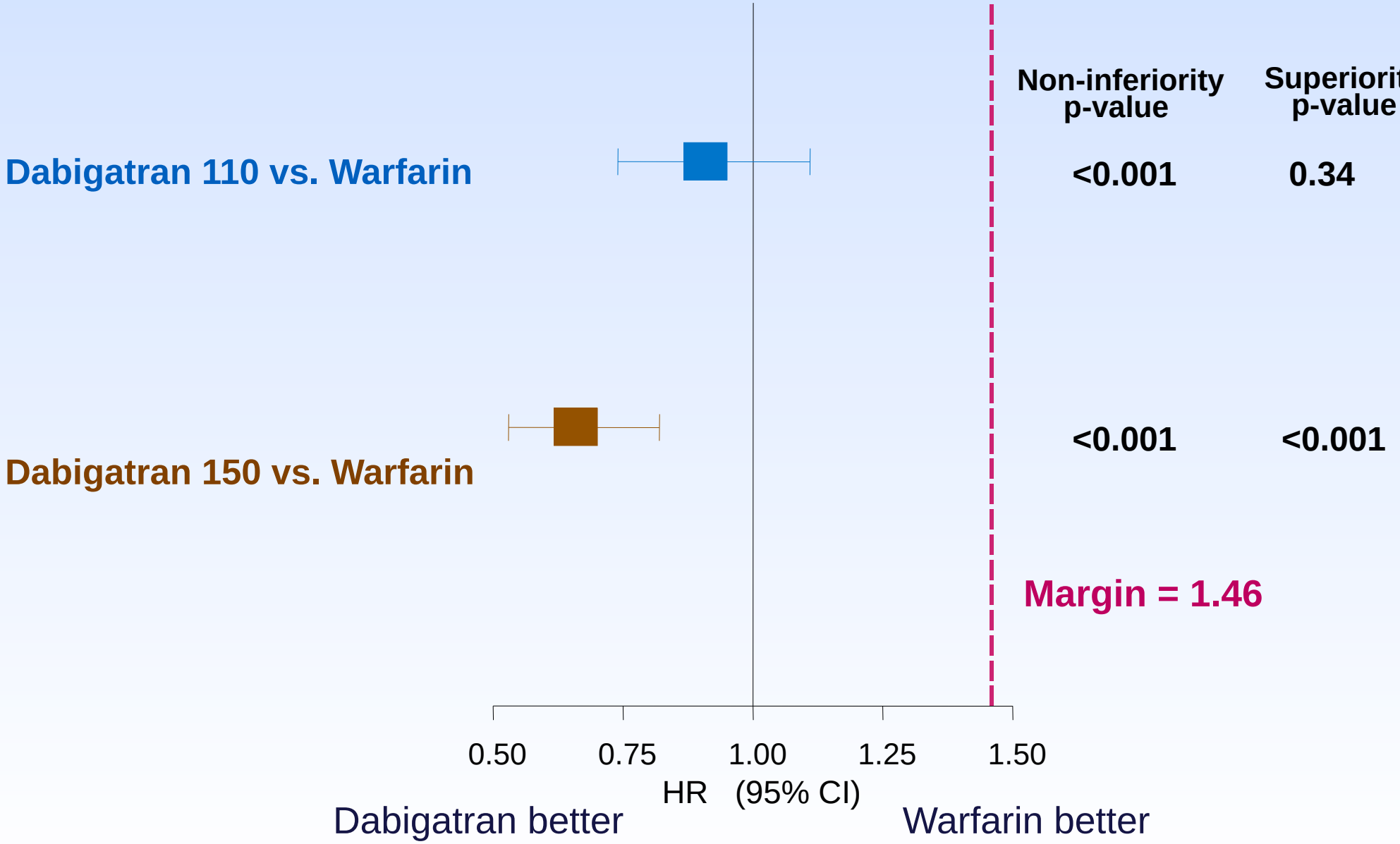
RE-LY: A Non-inferiority Trial

RELY®
Study of stroke prevention in atrial fibrillation



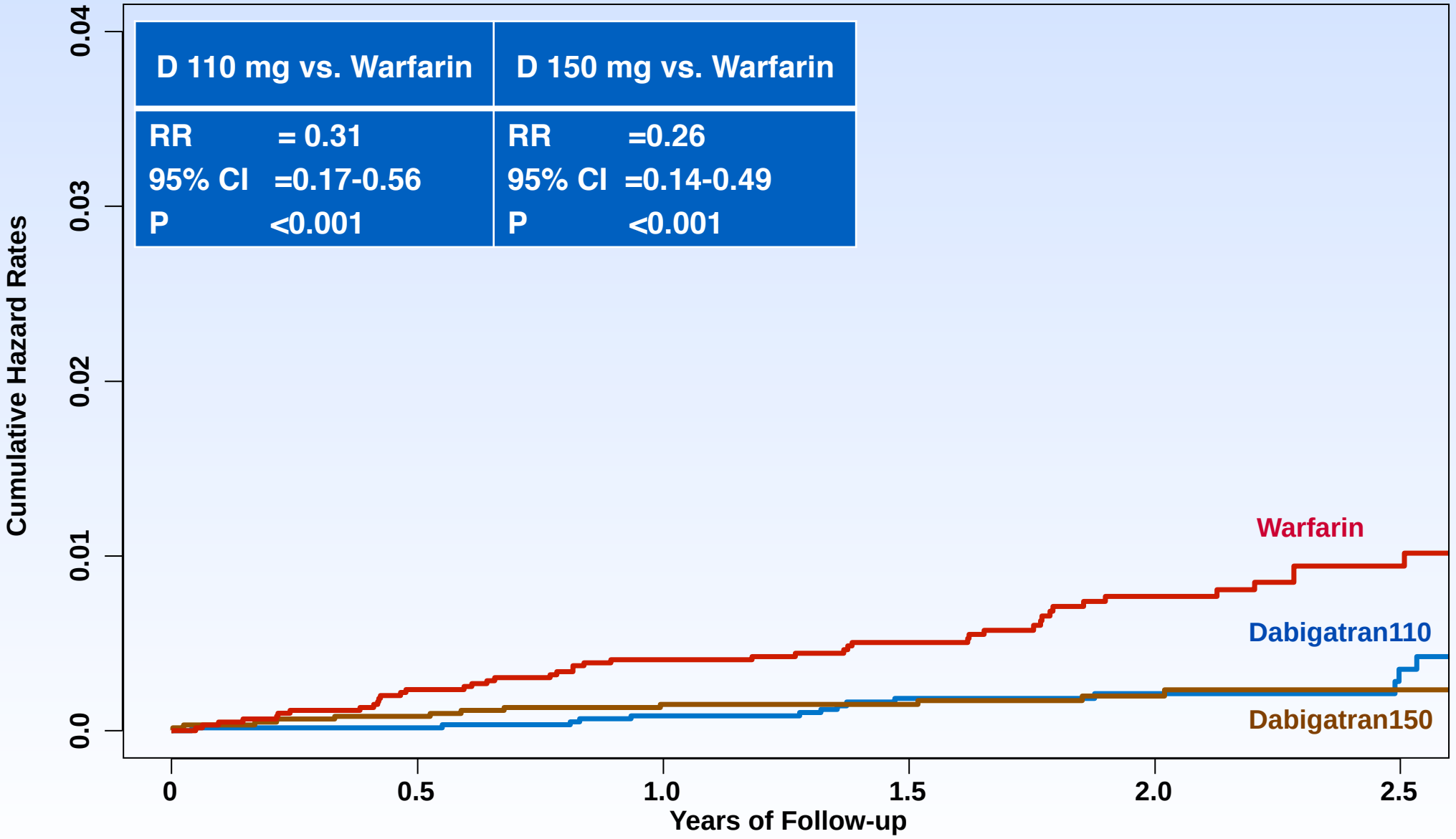
Stroke or Systemic Embolism

RELY®
Study of stroke prevention in atrial fibrillation



Hemorrhagic Stroke

RELY®
Study of stroke prevention in atrial fibrillation



Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial

*David R Holmes, Vivek Y Reddy, Zoltan G Turi, Shephal K Doshi, Horst Sievert, Maurice Buchbinder, Christopher M Mullin, Peter Sick, for the PROTECT AF Investigators**

Lancet 2009; 374: 534–42

See Editorial page 501

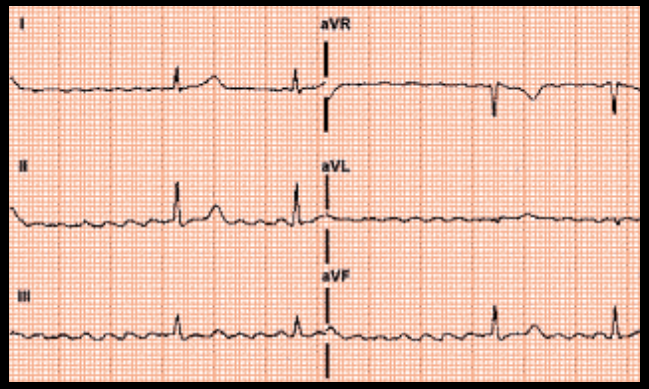
See Comment page 504

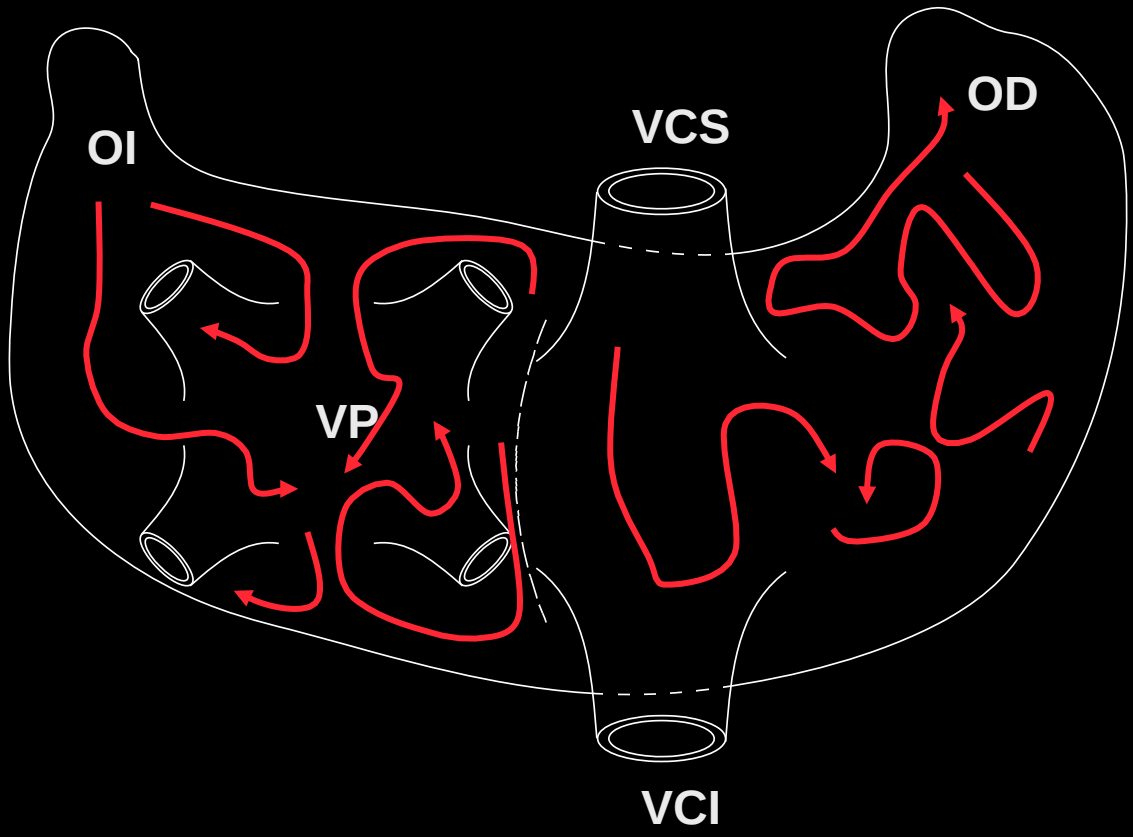
Summary

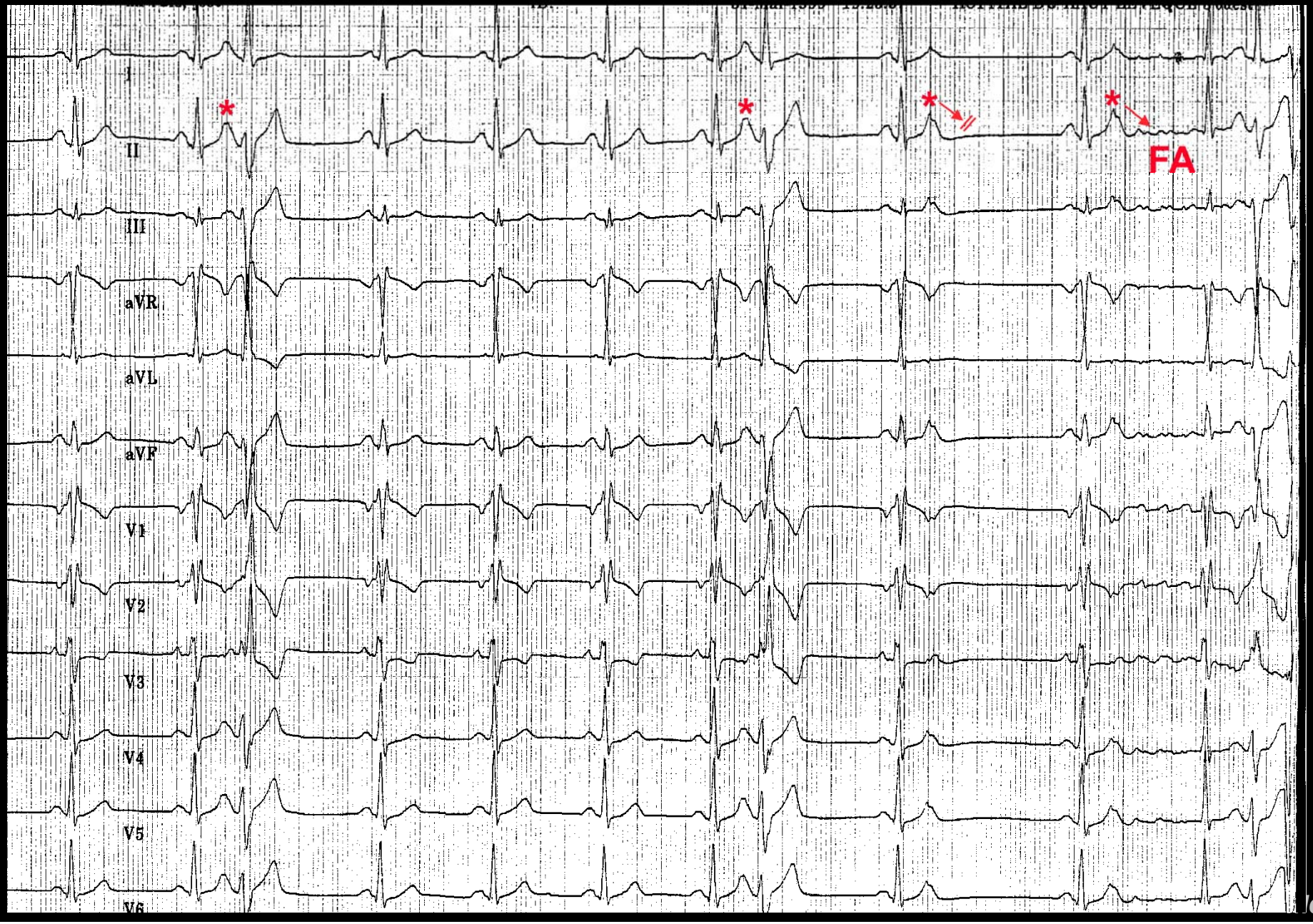
Background In patients with non-valvular atrial fibrillation, embolic stroke is thought to be associated with left atrial appendage (LAA) thrombi. We assessed the efficacy and safety of percutaneous closure of the LAA for prevention of stroke compared with warfarin treatment in patients with atrial fibrillation.

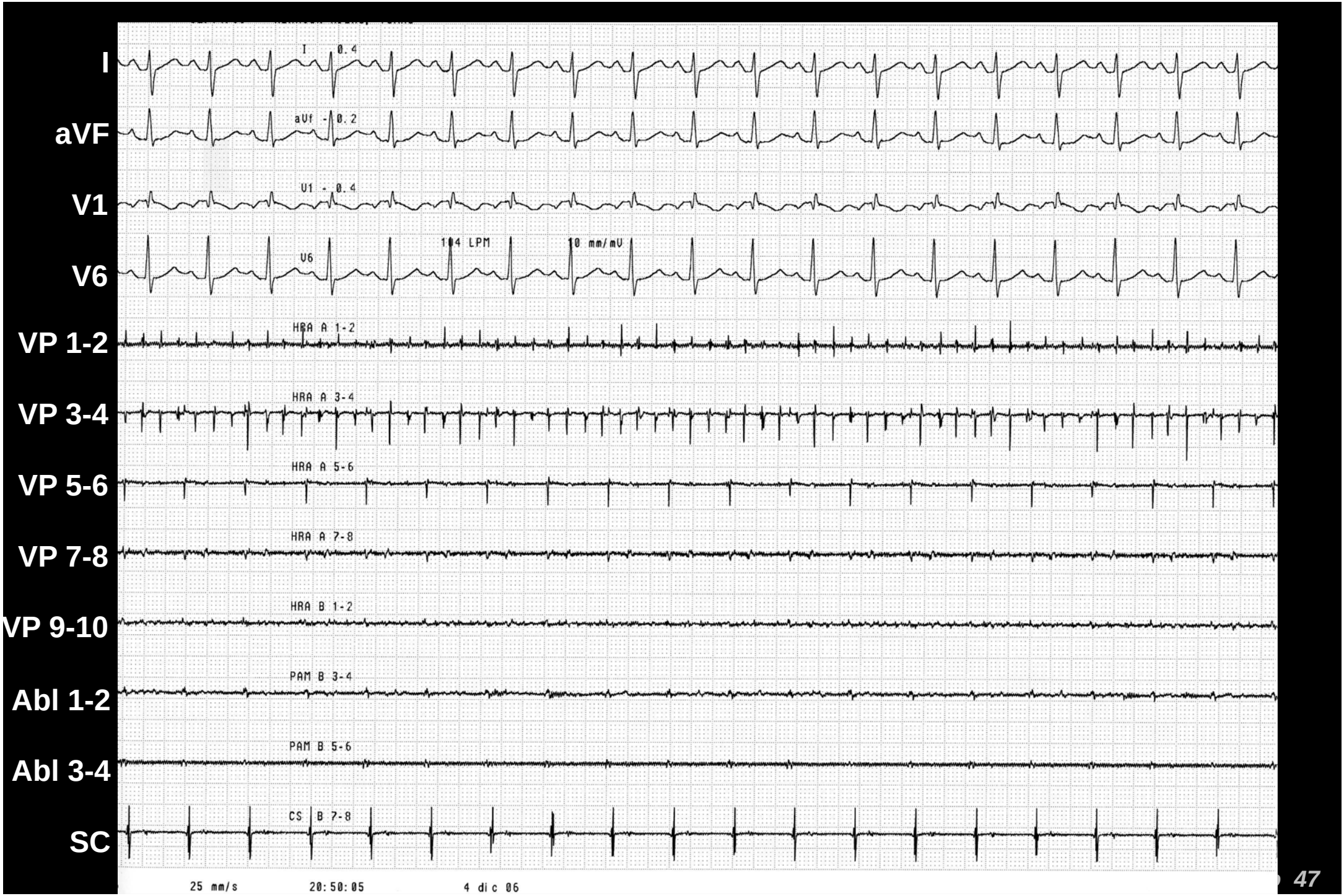
Ablación

¿Ablación primaria FA?

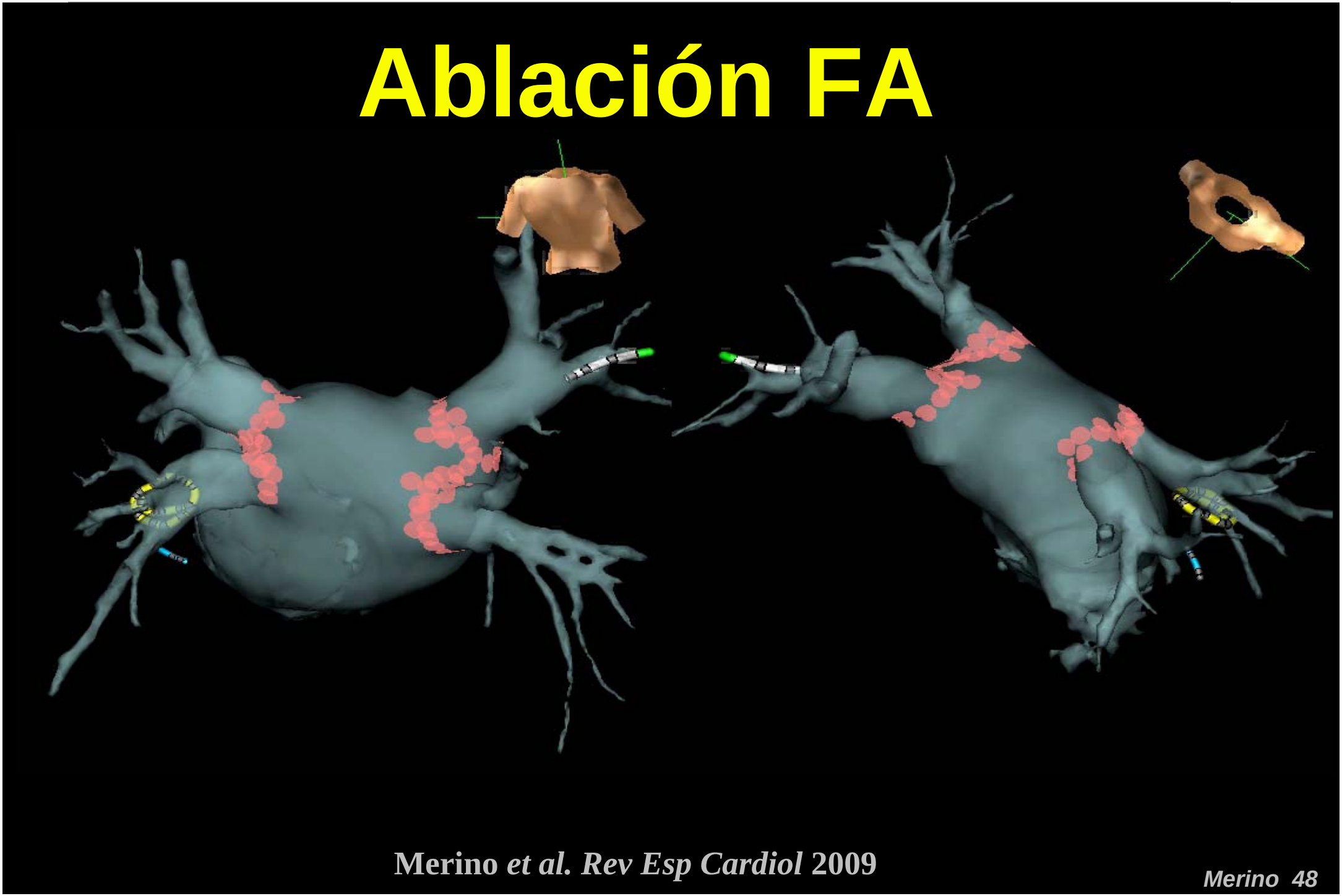





I
II
III
aVR
aVL
aVF
V1
V2
V3
V4
V5
V6
FA

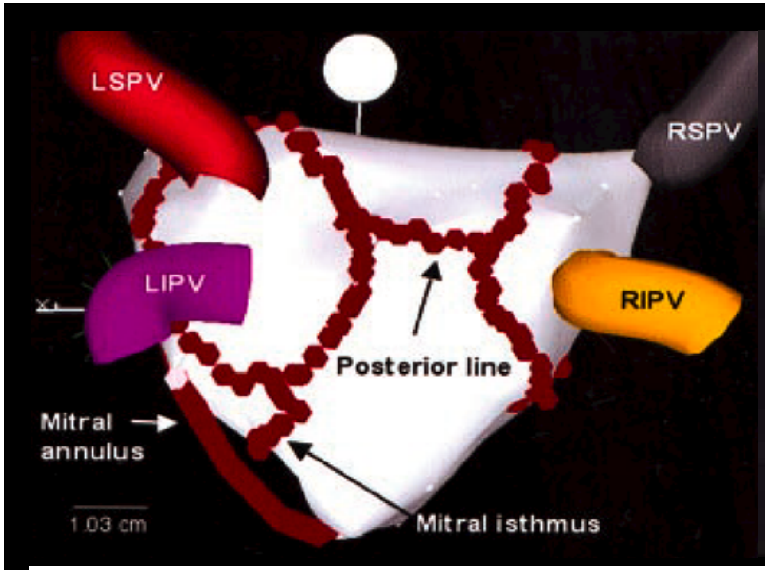

I
aVF
V1
V6
VP 1-2
VP 3-4
VP 5-6
VP 7-8
VP 9-10
Abl 1-2
Abl 3-4
SC
I 0.4
aVf - 0.2
V1 - 0.4
V6
104 LPM
10 mm/mV
HRA A 1-2
HRA A 3-4
HRA A 5-6
HRA A 7-8
HRA B 1-2
PAM B 3-4
PAM B 5-6
CS B 7-8
25 mm/s
20:50:05
4 dic 06

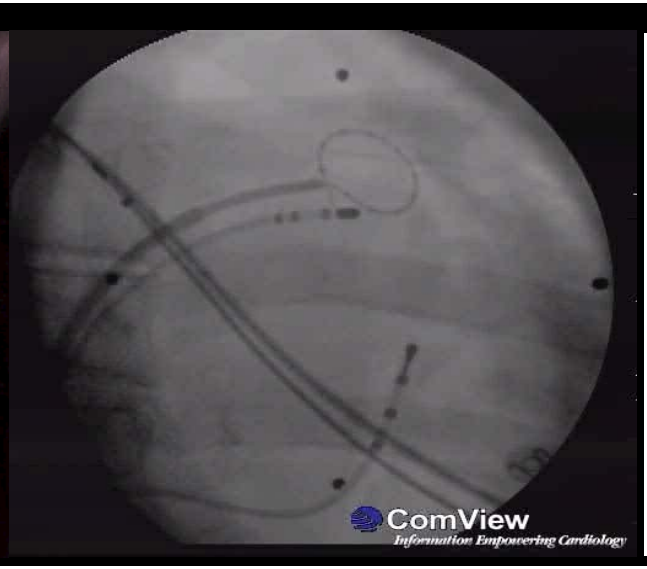
Ablación FA



Merino *et al. Rev Esp Cardiol* 2009

Eficacia





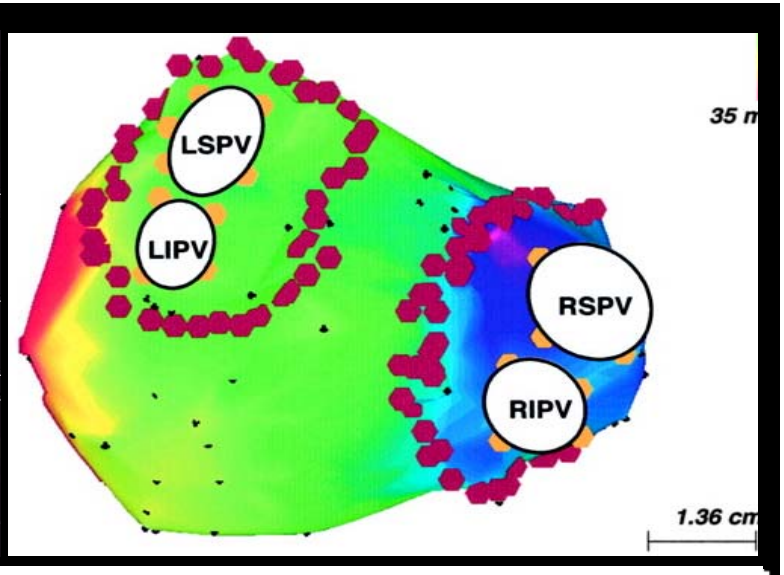


TABLE 1. Success Rates of Most Recent Studies Using Ablation of All PVs Outside the Tubular Segment

Study	Year	Patients	Age, y	Parox, %	SHD, %	Tool(s)	End Point	AF Free (Off Drugs), %	Follow-Up, d
Ouyang et al[37]	2004	41	63±9	100	NA	CARTO	PV Isolat'n	76*	178
Haissaguerre et al[38]	2004	70	53±8	NA	43	Fluoro	PV Isolat'n	79	210
Mansour et al[40]	2004	40	55±10	80	13	CARTO	PV Isolat'n	75	330
Marrouche et al[41]	2003	259	54±11	51	21	ICE	PV Isolat'n	87†	347
Oral et al[39]	2003	40	54±11	100	3	CARTO	EGM Red'n	88	365
Pappone et al[36]	2003	589	65±9	69	6	CARTO	EGM Red'n	79	861
Total									

Parox i
of local el
*Succe
†Succe

EGM Red'n, reduction
ebster).

En torno al 80% sin recurrencias y sin fármacos antiarrítmicos

Estudios Aleatorizados

Radiofrequency Ablation vs Antiarrhythmic Drugs as First-line Treatment of Symptomatic Atrial Fibrillation

A Randomized Trial

Oussama M. Wazni, MD
Nassir F. Marrouche, MD
David O. Martin, MD
Atul Verma, MD
Mandeep Bhargava, MD
Walid Saliba, MD
Dianna Bash, RN
Robert Schweikert, MD
Johannes Brachmann, MD
Jens Gunther, MD
Klaus Gutleben, MD
Ennio Pisano, MD
Dominico Potenza, MD
Raffaele Fanelli, MD
Antonio Raviele, MD
Sakis Themistoclakis, MD
Antonio Rossillo, MD
Aldo Bonso, MD
Andrea Natale, MD

Context Treatment with antiarrhythmic drugs and anticoagulation is considered first-line therapy in patients with symptomatic atrial fibrillation (AF). Pulmonary vein isolation (PVI) with radiofrequency ablation may cure AF, obviating the need for antiarrhythmic drugs and anticoagulation.

Objective To determine whether PVI is feasible as first-line therapy for treating patients with symptomatic AF.

Design, Setting, and Participants A multicenter prospective randomized study conducted from December 31, 2001, to July 1, 2002, of 70 patients aged 18 to 75 years who experienced monthly symptomatic AF episodes for at least 3 months and had not been treated with antiarrhythmic drugs.

Intervention Patients were randomized to receive either PVI using radiofrequency ablation (n=33) or antiarrhythmic drug treatment (n=37), with a 1-year follow-up.

Main Outcome Measures Recurrence of AF, hospitalization, and quality of life assessment.

Results Two patients in the antiarrhythmic drug treatment group and 1 patient in the PVI group were lost to follow-up. At the end of 1-year follow-up, 22 (63%) of 35 patients who received antiarrhythmic drugs had at least 1 recurrence of symptomatic AF compared with 4 (13%) of 32 patients who received PVI ($P<.001$). Hospitalization during 1-year follow-up occurred in 19 (54%) of 35 patients in the antiarrhythmic drug group compared with 3 (9%) of 32 in the PVI group ($P<.001$). In the antiarrhythmic drug group, the mean (SD) number of AF episodes decreased from 12 (7) to 6 (4), after initiating therapy ($P=.01$). At 6-month follow-up, the improvement in quality of life of patients in the PVI group was significantly better than the improvement in the antiarrhythmic drug group in 5 subclasses of the Short-Form 36 health survey. There were no thromboembolic events in either group. Asymptomatic mild or moderate pulmonary vein stenosis was documented in 2 (6%) of 32 patients in the PVI group.

Conclusion Pulmonary vein isolation appears to be a feasible first-line approach for treating patients with symptomatic AF. Larger studies are needed to confirm its safety and efficacy.

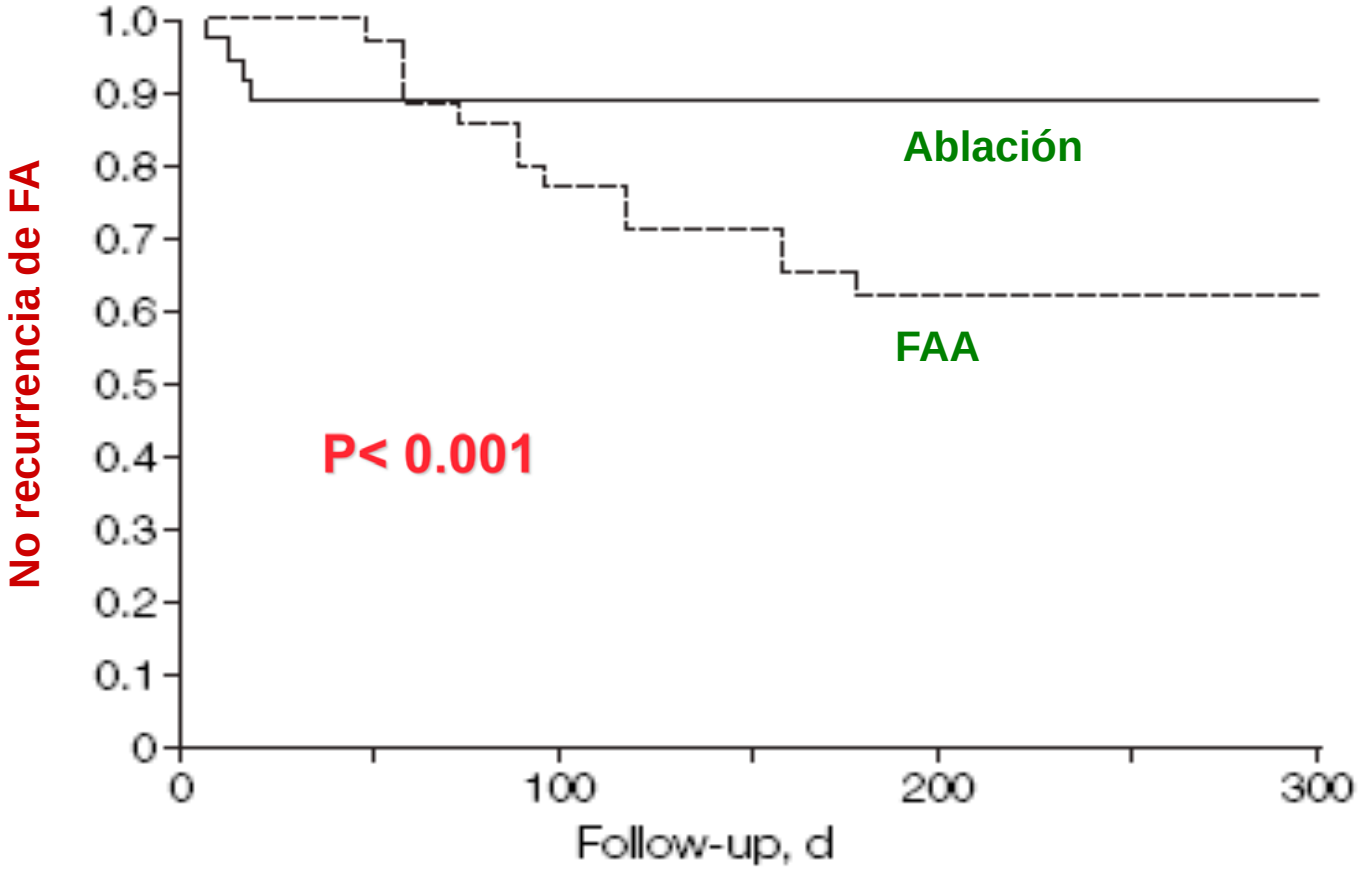
JAMA. 2003;289:2034-2040 www.jama.com

ATRIAL FIBRILLATION (AF), which affects approximately 2 million people in the United States, is a major cause of stroke, adversely impacts quality of life, and is associated with increased mor-

18-75 años

≥ 3 episodios de FA no tratados con FAA

Ablación FA vs FAA



No. at Risk							
PVI Group	32	28	28	28	28	28	28
Antiarrhythmic Drug Group	35	34	23	19	13	13	13

JAMA 2005; 293:2634-40

REVISTA ESPAÑOLA DE CARDIOLOGIA

ARTÍCULOS ESPECIALES

Registro Español de Ablación con Catéter. I Informe Oficial de la Sección de Electrofisiología y Arritmias de la Sociedad Española de Cardiología (Año 2001)

Miguel Álvarez y José L. Merino

Sección de Electrofisiología y Arritmias. Sociedad Española de Cardiología. Madrid. España.

ARTÍCULO ESPECIAL

Registro Español de Ablación con Catéter. VII Informe Oficial de la Sección de Electrofisiología y Arritmias de la Sociedad Española de Cardiología (2007)

Ignacio García-Bolao, Ernesto Díaz-Infante y Alfonso Macías Gallego

Sección de Electrofisiología y Arritmias. Sociedad Española de Cardiología. Madrid. España.

Registro Español Ablación *2007*

- **Complicaciones: 5,4%**
  - **Derrame P 3,2%**
  - **ACV/emb coronaria 0,8%**
  - **Vascular 0,8%**

European Heart Journal (2006) 27, 1979–2030
doi:10.1093/eurheartj/ehl176

ACC/AHA/ESC Guidelines

ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation—executive summary

A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients with Atrial Fibrillation)
Developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society

Abl FA

4. Maintenance of sinus rhythm

Class I

Before initiating antiarrhythmic drug therapy, treatment of precipitating or reversible causes of AF is recommended. *(Level of Evidence: C)*

Class IIa

(1) Pharmacological therapy can be useful in patients with AF to maintain sinus rhythm and prevent tachycardia-

(2) Infrequent, well-tolerated recurrence of AF is reasonable as a successful outcome of antiarrhythmic drug therapy. *(Level of Evidence: C)*

(3) Outpatient initiation of antiarrhythmic drug therapy is reasonable in patients with AF who have no associated heart disease when the agent is well tolerated. *(Level of Evidence: C)*

(4) In patients with lone AF without structural heart disease, initiation of propafenone or flecainide can be beneficial on an outpatient basis in patients with paroxysmal AF who are in sinus rhythm at the time of drug initiation. *(Level of Evidence: B)*

(5) Sotalol can be beneficial in outpatients in sinus rhythm with little or no heart disease, prone to paroxysmal AF, if the baseline uncorrected QT interval is less than 460 ms, serum electrolytes are normal, and risk factors associated with class III drug-related proarrhythmia are not present. *(Level of Evidence: C)*

(6) Catheter ablation is a reasonable alternative to pharmacological therapy to prevent recurrent AF in symptomatic patients with little or no LA enlargement. *(Level of Evidence: C)*

Any modifications to the components of this Patient Informed Consent Form must be reviewed by the PHRI Canada before local Research Ethics Board (REB) submission. Any changes requested by your local REB following the review process must also be reviewed by the PHRI. Please ensure that your study coordinator sends any changes to Rashid Ahmed, central RAAFT study coordinator rashid@phri.ca

Con formato

Hamilton General Hospital

(insert your hospital letterhead with logo and address here)

RAAFT TRIAL

First Line Radiofrequency Ablation versus Antiarrhythmic Drugs for Atrial Fibrillation Treatment: A Multi-center Randomized Trial

Eliminado: ¶

INVESTIGATORS: Dr. Carlos Morillo, Dr. Stuart Connolly, Dr. Jeffry Healey, Dr. Girish Nair, Dr. Syamkumar Divakaramenon, Dr. Pablo Neary.

SPONSOR: Hamilton Health Sciences Corporation through Population Health Research Institute

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PATIENT INFORMATION SHEET AND CONSENT FORM

¿Un Futuro para los FAA?

FAA en FA

- Ablación en desarrollo *(no es clase I)*
- Algunos FAA mejoran pronóstico
- Manejo agudo arritmias
- Prevalencia FA (≈1%)

FAA seguirán en el futuro

Conclusiones

- FAA están para quedarse:
  - Manejo agudo de FA
  - Complemento Ablación
  - Prevalencia FA
- Nuevos antitromboticos y estrategias
- Ablación:
  - Opción real clara
  - Desarrollo tecnológico tremendo
- Estrategias prevención