

# Estudio SHARP

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## Implicaciones en la Prevención 2ª de la Cardiopatía Isquémica

1

**José R. González Juanatey**

**Área Cardiovascular. Hospital Clínico Universitario de Santiago de  
Compostela**

# Ezetimibe 2011

## Cuestiones pendientes

Eficacia

Seguridad

Nefroprotección

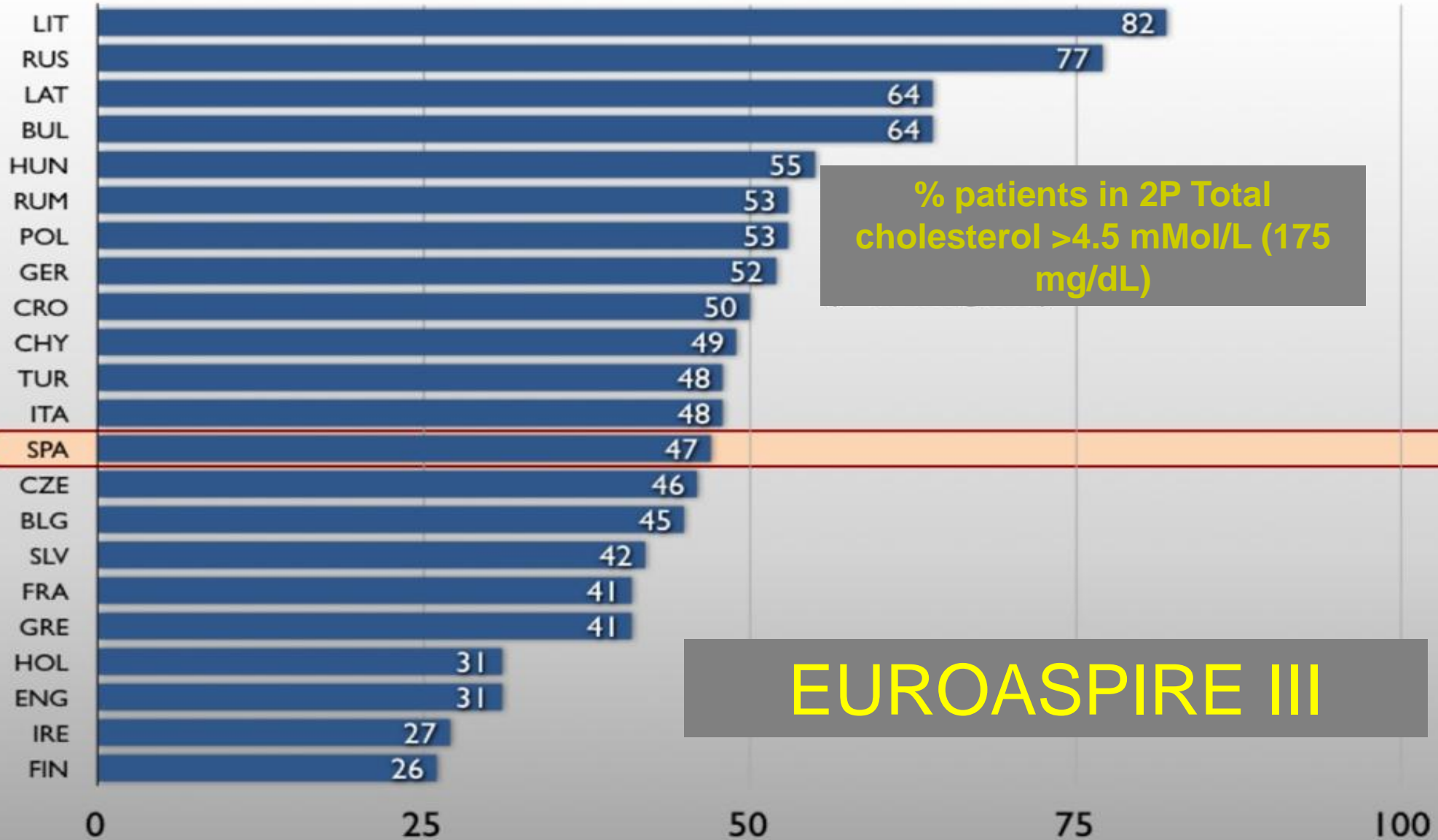
# FRC INTERHEART



Yusuf S, Hawken S, Ounpuu S, on behalf of the INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries: case-control study. Lancet. 2004;364:937-952.

• Rosengren A, Hawken S, Ounpuu S, et al, for the INTERHEART investigators. Association of psychosocial risk factors with risk of acute myocardial infarction in 11 119 cases and 13 648 controls from 52 countries: case-control study. Lancet. 2004;364:953-962.2.

# EU, Total Cholesterol Goal

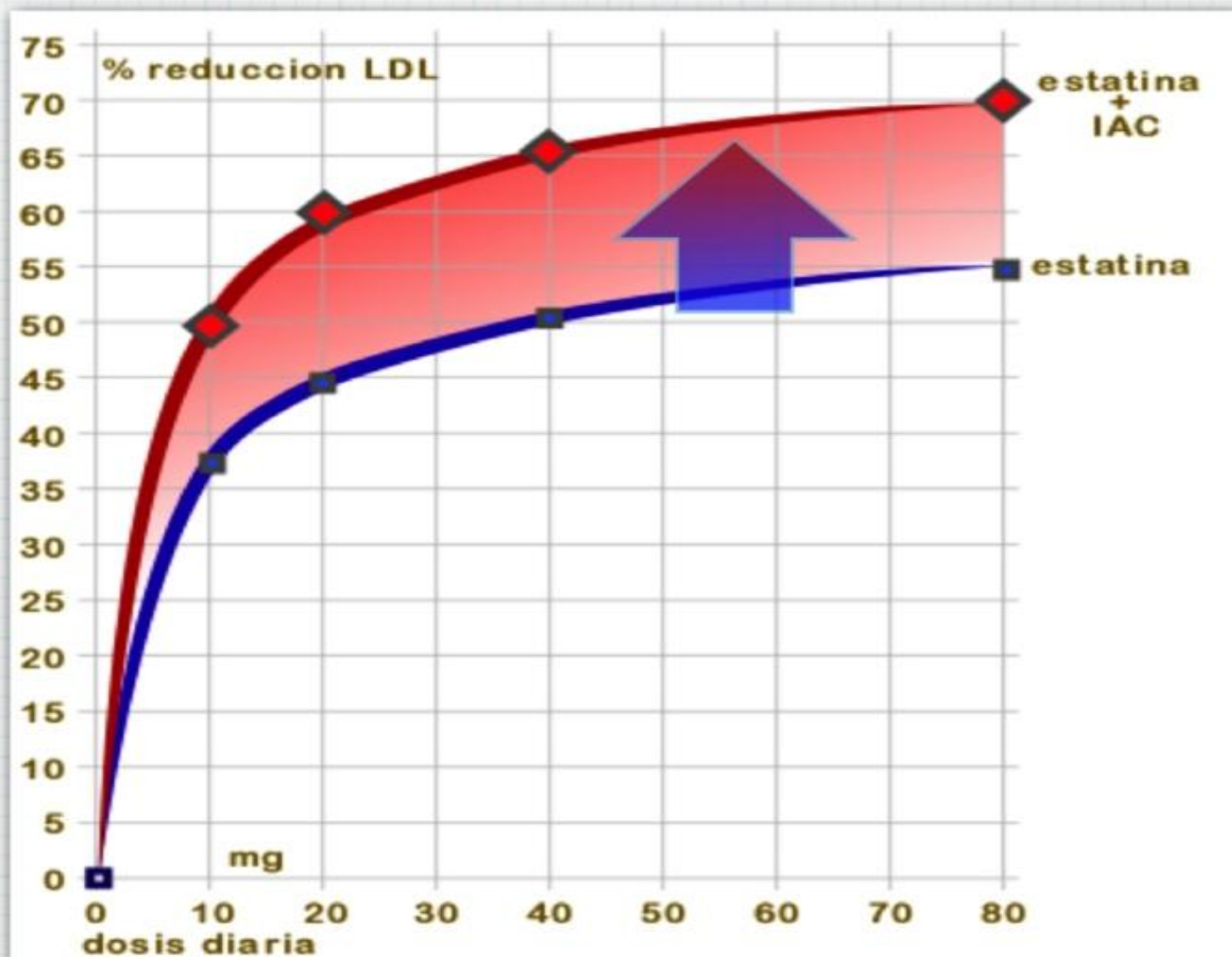


% patients in 2P Total cholesterol >4.5 mMol/L (175 mg/dL)

EUROASPIRE III



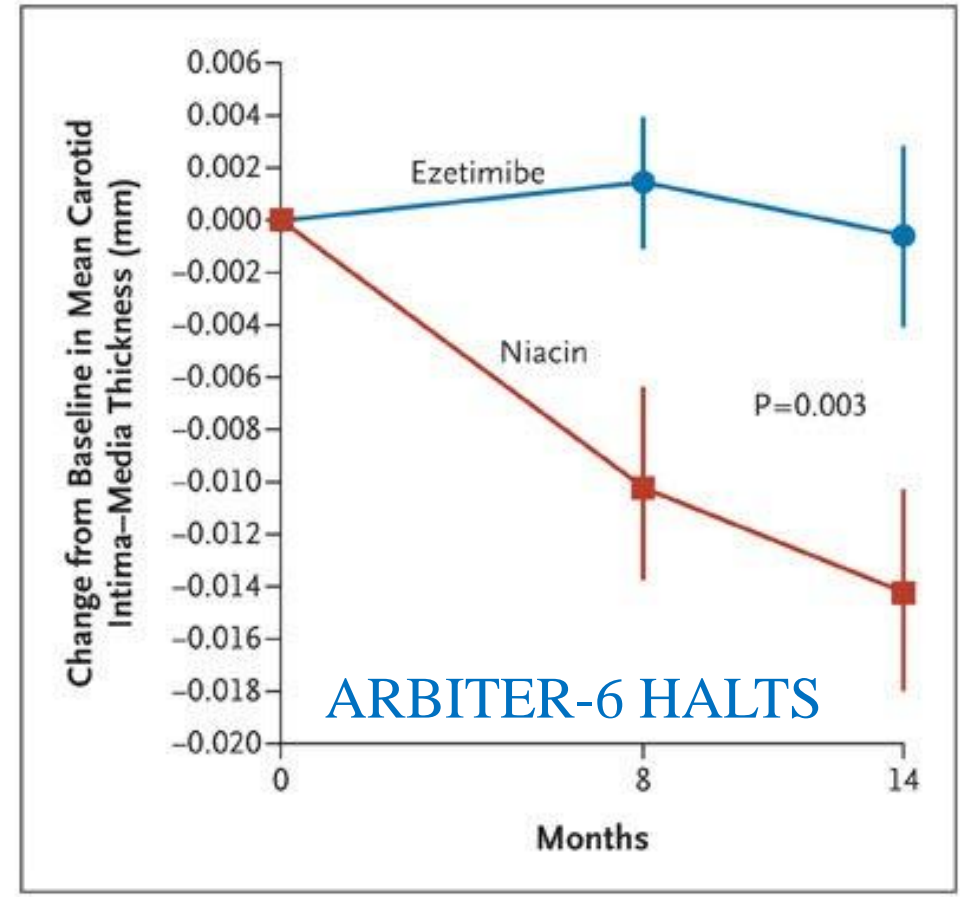
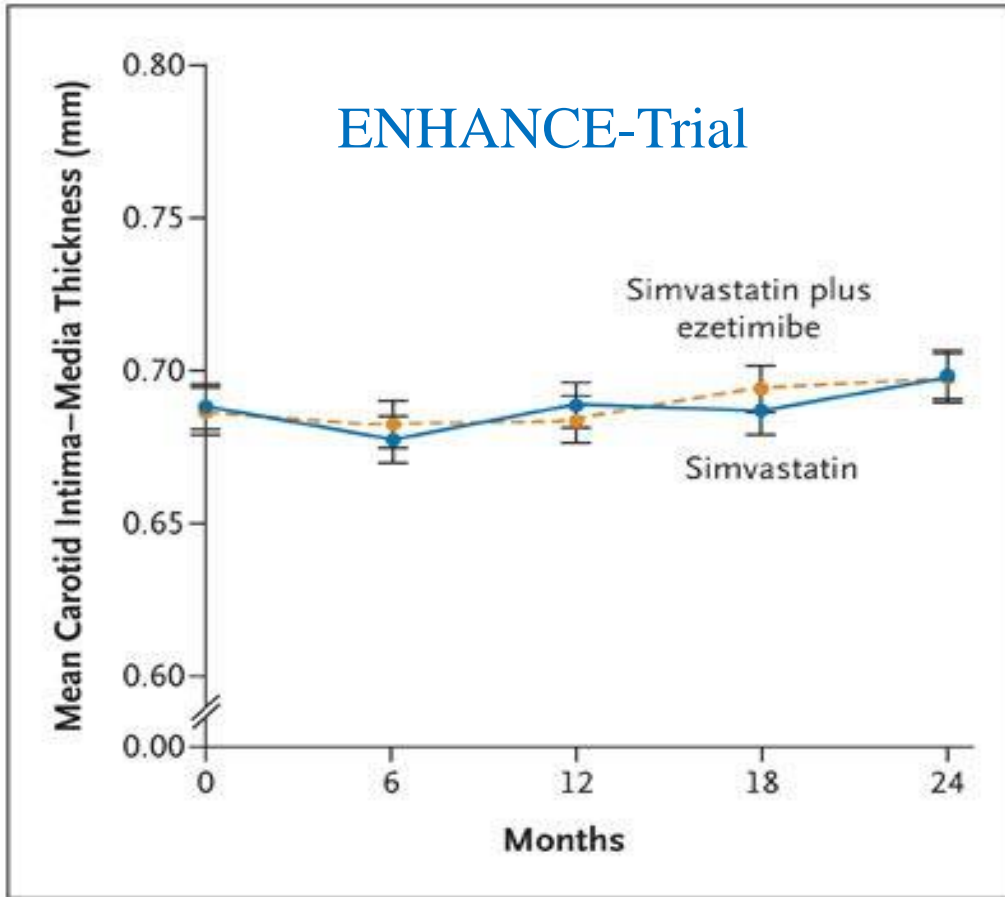
# asociar IAC y STA



# estatina y ezetimibe



# Intima-Media Thickness of the Carotid Artery during 24 and 14 Months of Therapy



Kastelein J et al. N Engl J Med 2008;358:1431-1443

Taylor A et al. N Engl J Med 2009;361:2113-2122



# Ezetimibe

## Drugs

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### Drug Safety and Availability

#### Postmarket Drug Safety Information for Patients and Providers

#### Drug Safety Information for Healthcare Professionals

Communications about Ongoing Safety Reviews

Early Communications About

## Follow-Up to the August 2008 Early Communication About an Ongoing Safety Review of Ezetimibe/Simvastatin (marketed as Vytorin), Simvastatin (marketed as Zocor) and Ezetimibe (marketed as Zetia) - FDA Investigates a Report from the SEAS Trial

[12-22-2009] In August 2008, the U.S. Food and Drug Administration (FDA) issued an Early Communication describing a possible association between the use of Vytorin – a combination of simvastatin (Zocor) and ezetimibe (Zetia) – and an increased risk of cancer and cancer-related

“During the trial, investigators reported an increased number of cancers and cancer-related deaths in patients using Vytorin compared to placebo. Cancer was reported in 105 patients (11.1%) in the Vytorin group and in 70 patients (7.5%) in the placebo group. The number of deaths from cancer was also higher in the Vytorin group, with 39 deaths compared to 23 deaths in the placebo group.

A large body of long-term clinical data indicates that **simvastatin** is not associated with an increased risk of cancer, **but long-term clinical data on ezetimibe is insufficient to definitely rule out a cancer risk at this time.**”



# Alternativas en práctica clínica

- **ESTATINA**  
a dosis elevada

- **ventajas**

- evidencia

- **inconvenientes**

- efectos secundarios

- **IAC+**

- ESTATINA a dosis común

- **ventajas**

- bajas dosis

- **inconvenientes**

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ambas alcanzan eficacia similar en cuanto a descensos del colesterol LDL

# de qué estamos pendientes...

- ▶ EZE...
  - ▶ IMPROVE-IT (2013)
  - ▶ SHARP
  
- ▶ NIA...
  - ▶ AIM-HIGH (2011)
  - ▶ HPS2-THRIVE (2013)

# Ezetimibe 2011

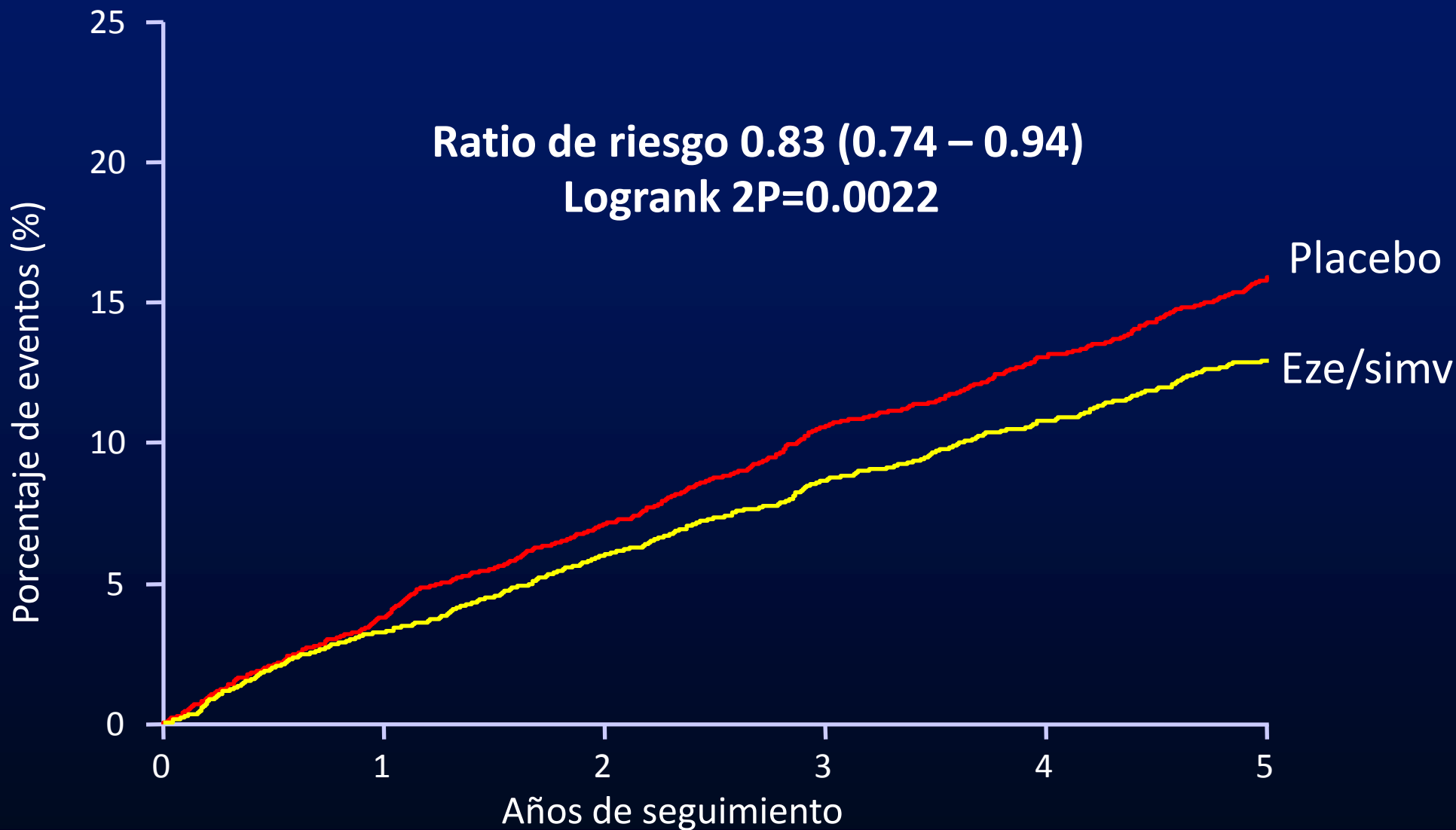
**Cuestiones pendientes**

**Eficacia**

**Seguridad**

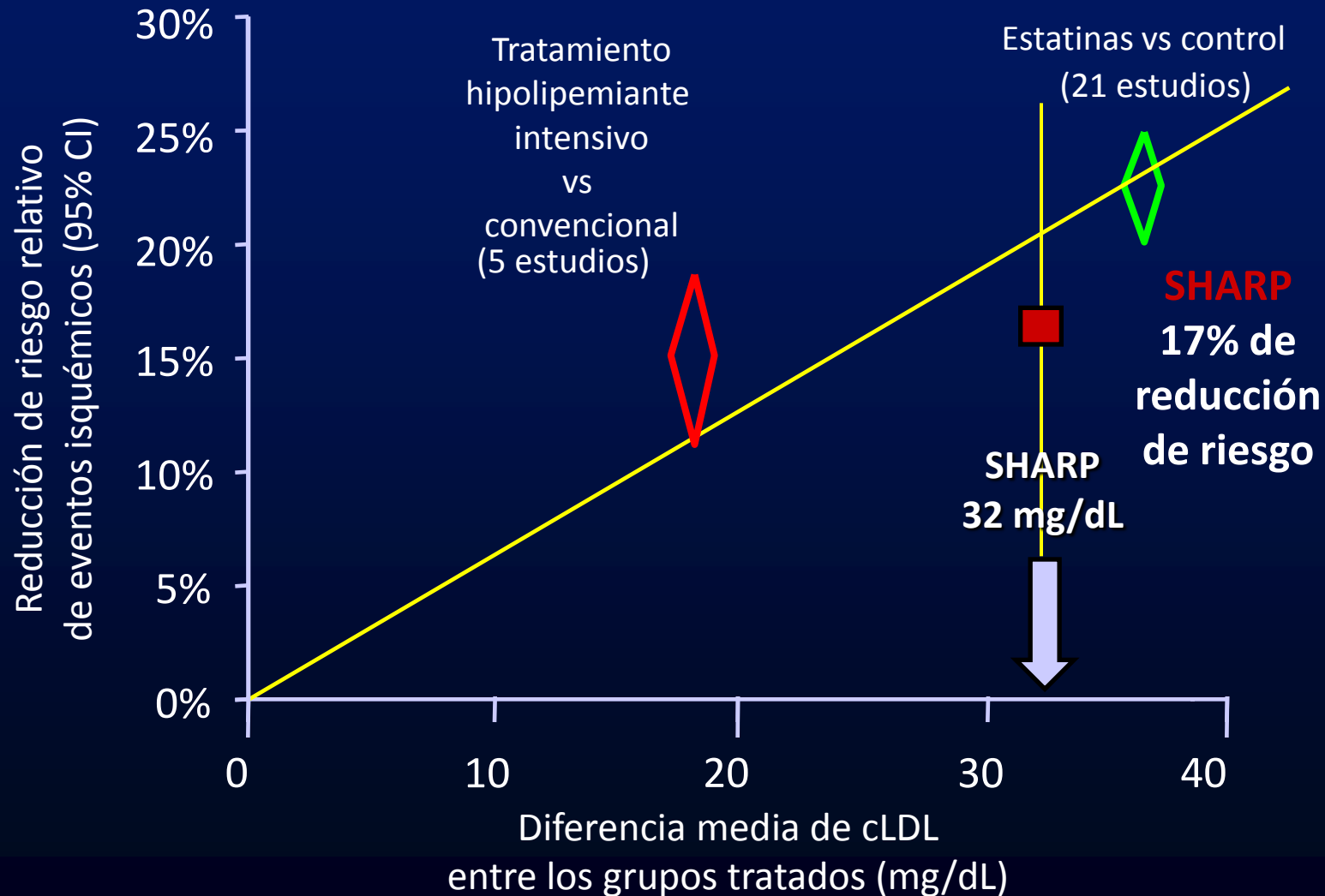
**Nefroprotección**

# SHARP: Principales eventos isquémicos





# CTT: Efectos sobre los eventos isquémicos

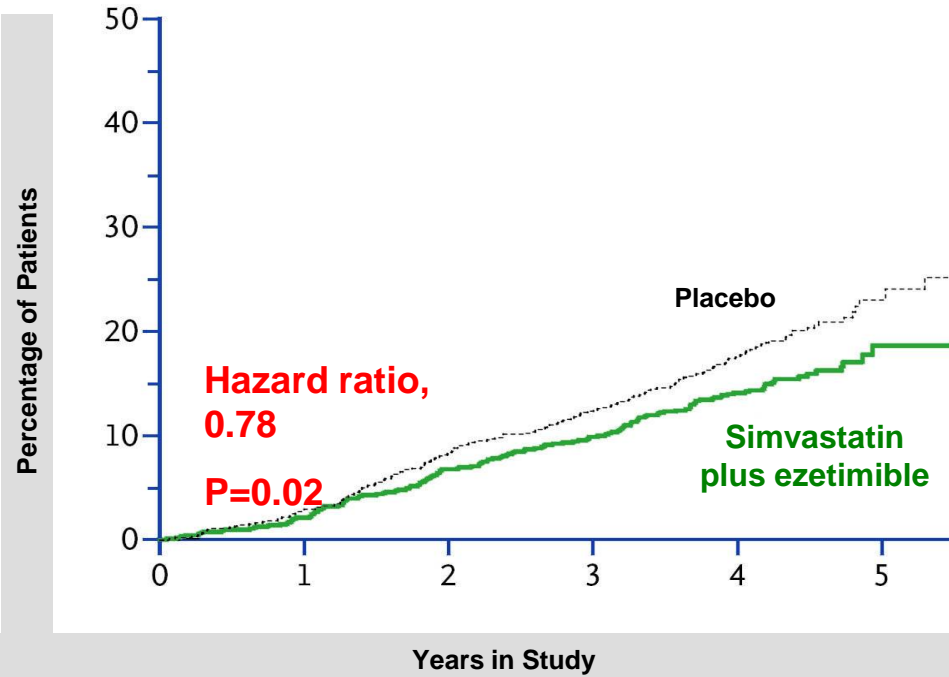


# Intensive Lipid Lowering with Simvastatin and Ezetimibe in Aortic Stenosis

## Kaplan–Meier Curves for Primary and Secondary Outcomes and Death

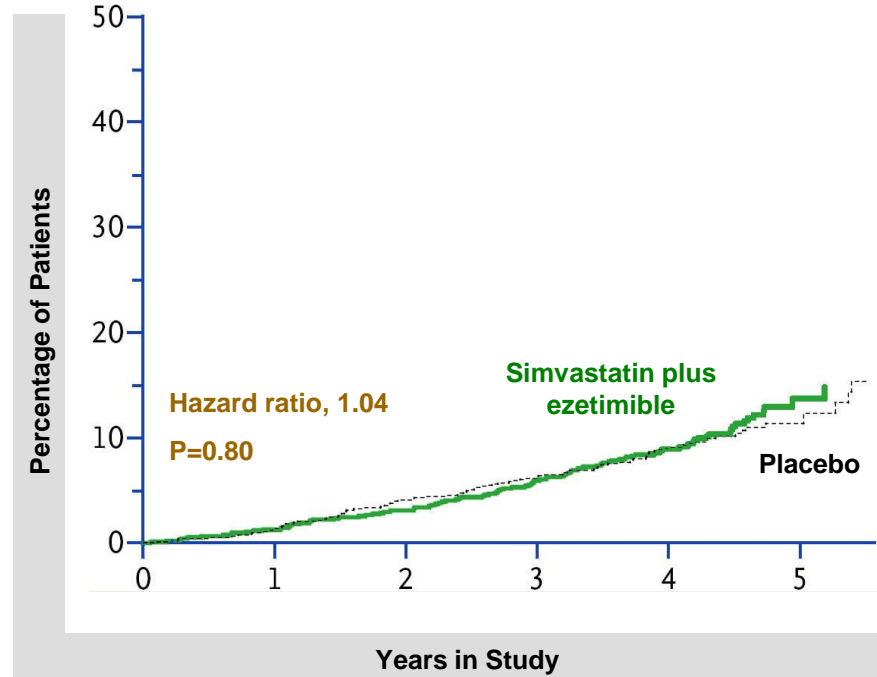
### Ischemic Cardiovascular Events

### Death from Any cause



#### No. at Risk

Simvastatin plus ezetimibe	917	867	823	769	76
Placebo	898	838	788	729	76



#### No. at Risk

Simvastatin plus ezetimibe	930	912	884	855	89
Placebo	916	890	865	835	94

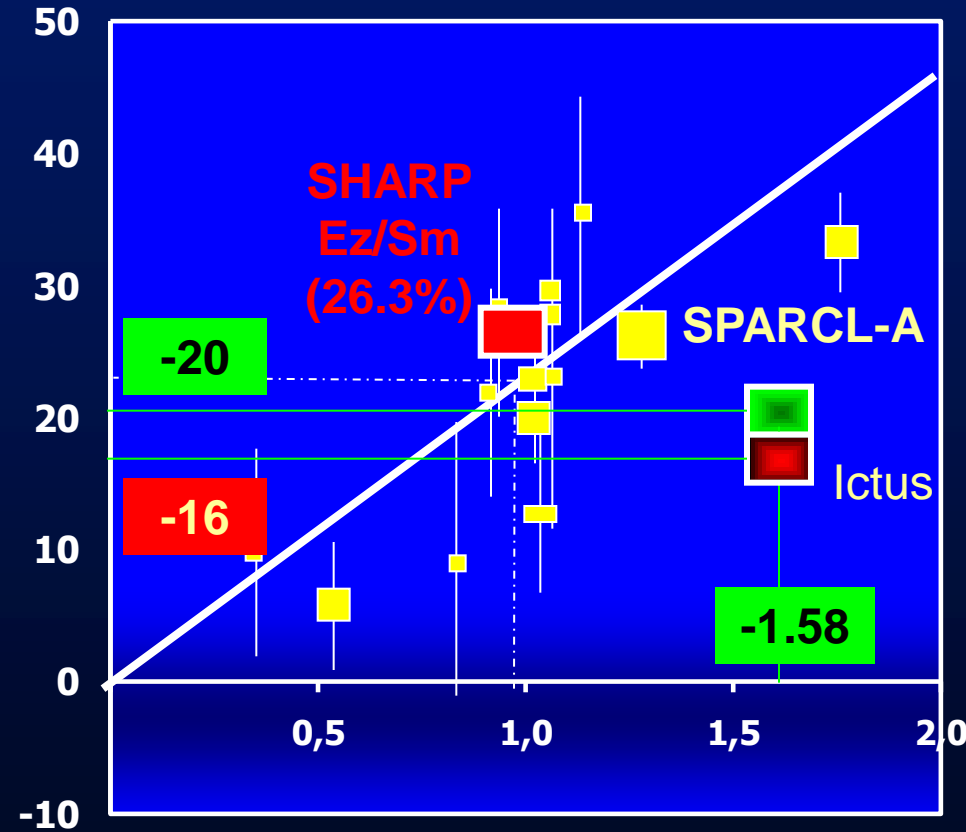
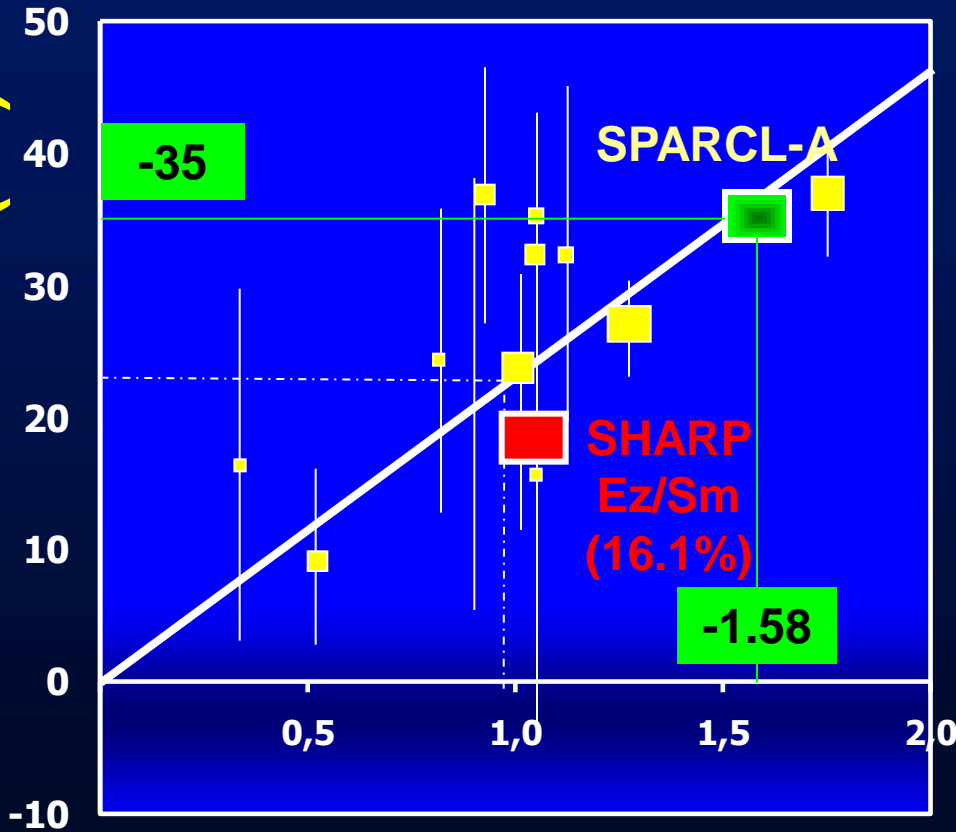
# Meta-análisis Hipolipemiantes

## Ez/Sim - Eficacia

Enfermedades Coronarias Mayores

Enfermedades Vasculares Mayores

Reducción Proporcional en Índice de Enfermedades (SE)



Reducción colesterol LDL (mmol/L)

Lancet 2006, 2010

# CTT:

2.5 y†

	Placebo	Ezetimibe plus simvastatin	P
	-8 (1)	-49 (1)	<.0001
	-6 (0.5)	-39 (0.6)	<.0001
	0 (0.2)	1 (0.2)	.21
Total cholesterol, mg/dL	-21 (1)	-45 (1)	<.0001
LDL cholesterol, mg/dL	-4 (0.4)	-27 (0.5)	<.0001
HDL cholesterol, mg/dL	8 (0.4)	10 (0.4)	.04
Triglycerides, mg/dL	-10 (3)	-21 (9)	<.0001
Apolipoprotein B, mg/dL	-1 (1)	-22 (2)	<.0001
Apolipoprotein A <sub>1</sub> , mg/dL	1 (1)	5 (2)	.01

# Eventos isquémicos

## CV Protection in CKD Pt

Estatinas vs control  
(21 estudios)



Baseline:

CT 189+45 mg/dl

LDL-C 108+34 mg/dl

entre los grupos tratados (mg/dL)



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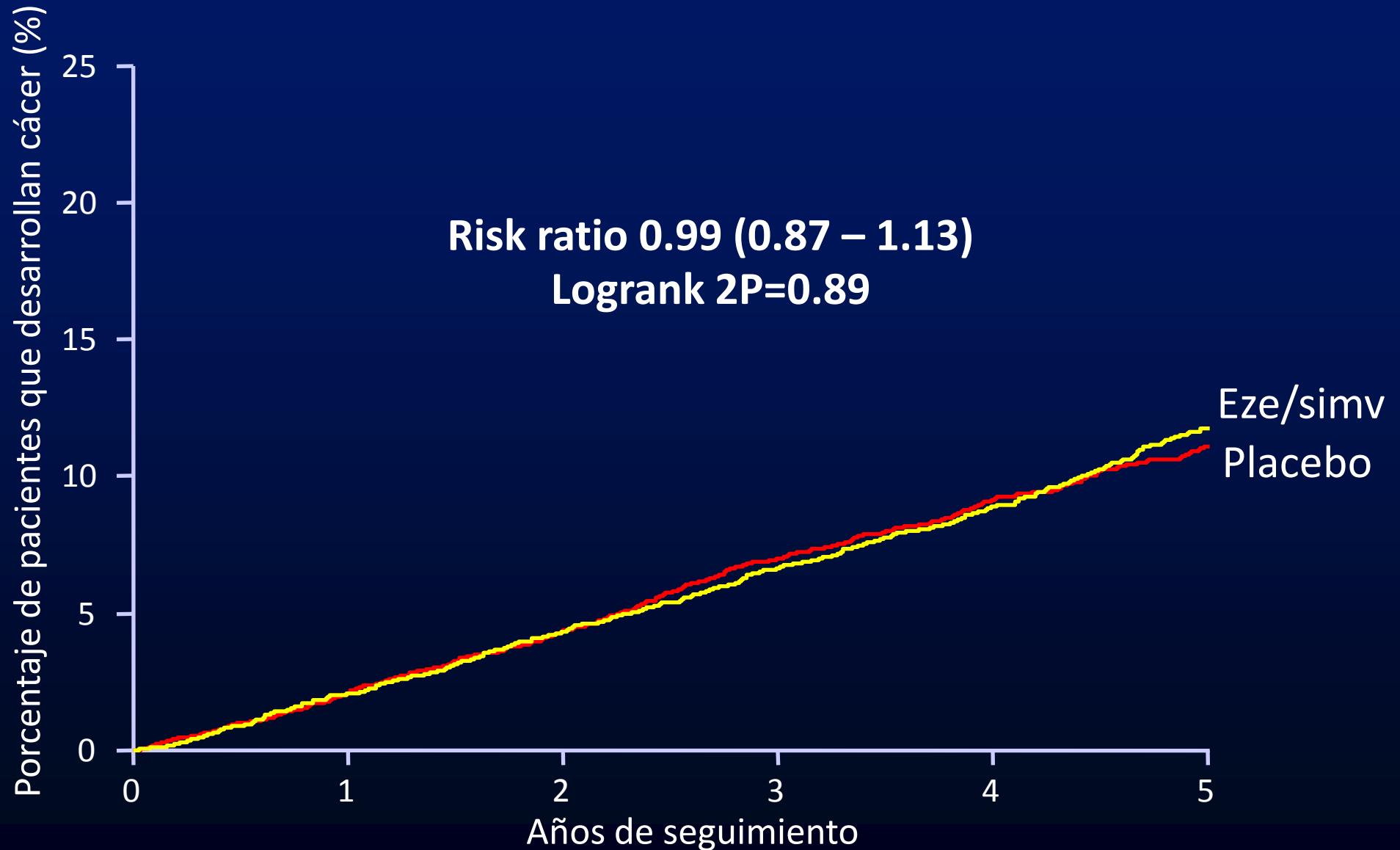
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# SHARP: Incidencia de Cáncer



# SHARP: Seguridad

	<b>Eze/simv</b> (n=4650)	<b>Placebo</b> (n=4620)
<b>Miopatía</b>		
<b>CK &gt;10 x y ≤40 x ULN</b>	17 (0.4%)	16 (0.3%)
<b>CK &gt;40 x ULN</b>	4 (0.1%)	5 (0.1%)
<b>Hepatitis</b>	21 (0.5%)	18 (0.4%)
<b>Aumento continuado ALT/AST &gt;3x ULN</b>	30 (0.6%)	26 (0.6%)
<b>Complicaciones por cálculos biliares</b>	85 (1.8%)	76 (1.6%)
<b>Otras hospitalizaciones por cálculos biliares</b>	21 (0.5%)	30 (0.6%)
<b>Pancreatitis sin cálculos biliares</b>	12 (0.3%)	17 (0.4%)





# Ezetimibe

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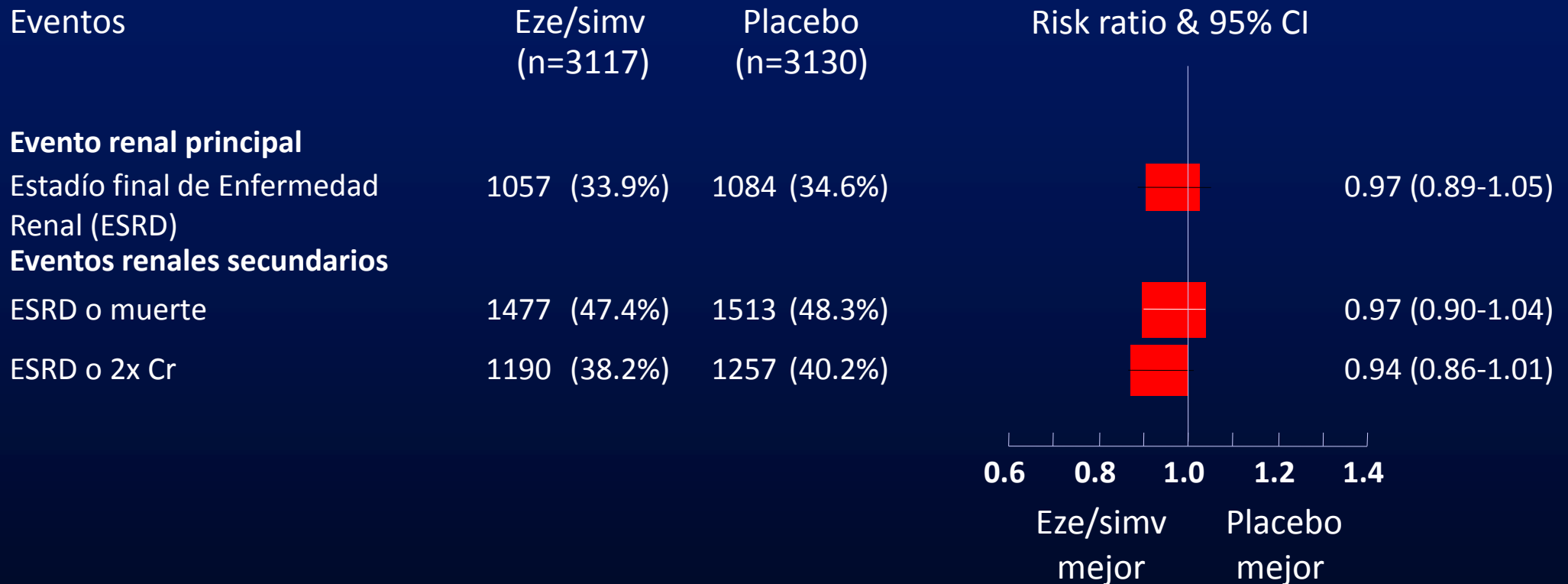
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# SHARP: Datos sobre parámetros Renales



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