

# 11 CONGRESO Societat Catalana de Trasplantament



**Barcelona**

**16-18 marzo 2011**

## CONTROVERSIA EN INMUNOSUPRESIÓN

**Calceurínicos: sí o no**

Piedad Ussetti, Madrid

# CONTROVERSIA EN INMUNOSUPRESIÓN

## MODERADORES:

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Juan Delgado, Madrid

Piedad Ussetti, Madrid



# Calcineurínicos si o no: Trasplante pulmonar



- Situación actual respecto a los INH
- ¿Deberían emplearse menos?
- ¿Por qué se siguen empleando?
- ¿Existen alternativas?

# REGISTRO ESPAÑOL DE TX PULMONAR

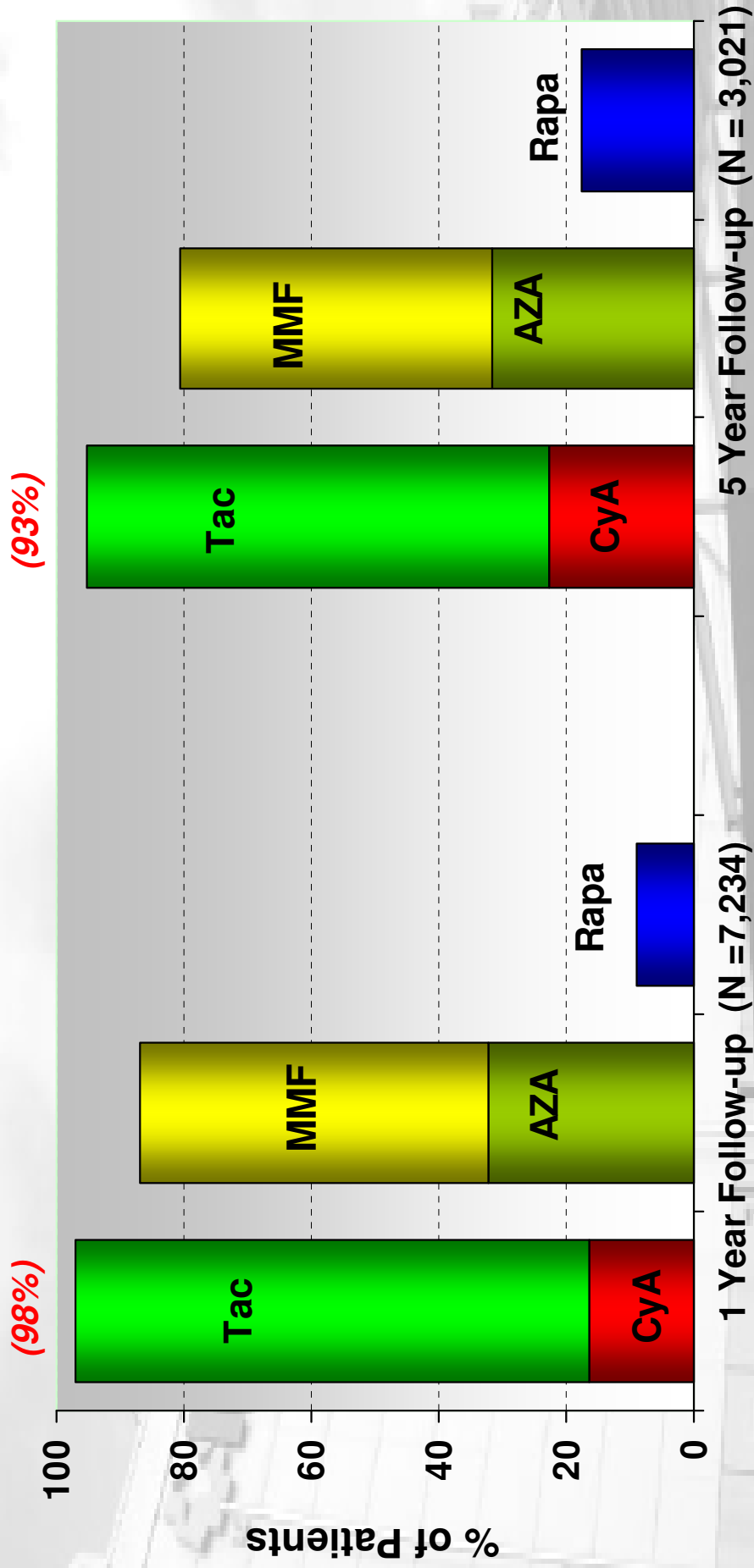
The screenshot shows the header of the website. On the left, there are logos for ONT (Organismo Nacional de Trasplantes), the Spanish Lung Transplant Register, and the Spanish Government. The main title is 'REGISTRO ESPAÑOL DE TRASPLANTE PULMONAR' in large white letters on a dark blue background. Below the title, it says 'Resultados 2006-2009'. At the top right of the page, there is a navigation link 'WEB ONT?'.

WEB ONT?

<https://portal.ont.es>

# ADULT LUNG RECIPIENTS

Maintenance Immunosuppression at Time of Follow-up  
For follow-ups between January 2002 through June 2009

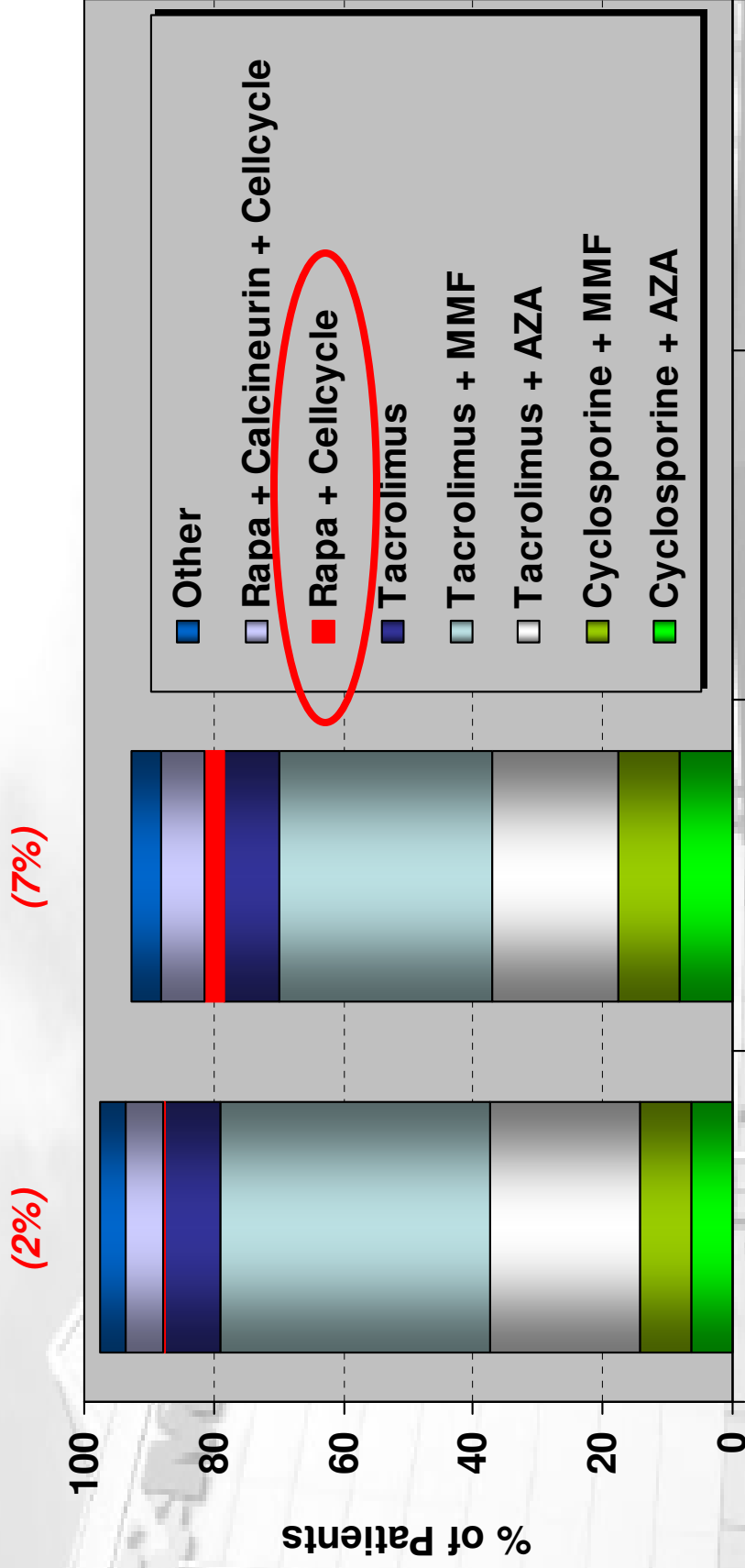


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2010

# ADULT LUNG RECIPIENTS

Maintenance Immunosuppression Drug Combinations at Time of Follow-up  
 For follow-ups between January 2002 through June 2009



Year 1 (N = 7,234)    Year 5 (N = 3,021)

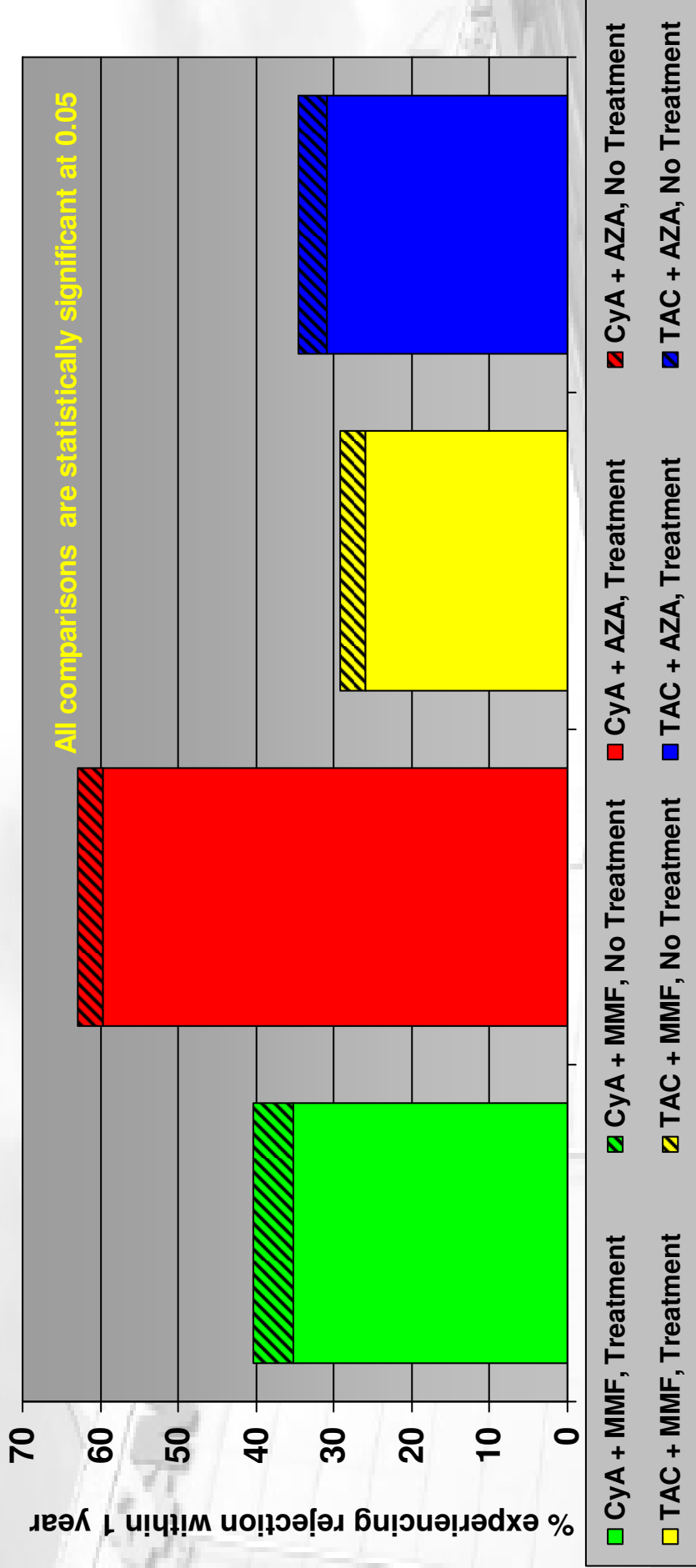


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# PERCENTAGE OF ADULT LUNG TRANSPLANT RECIPIENTS

## Experiencing Rejection between Transplant Discharge and 1-Year Follow-Up



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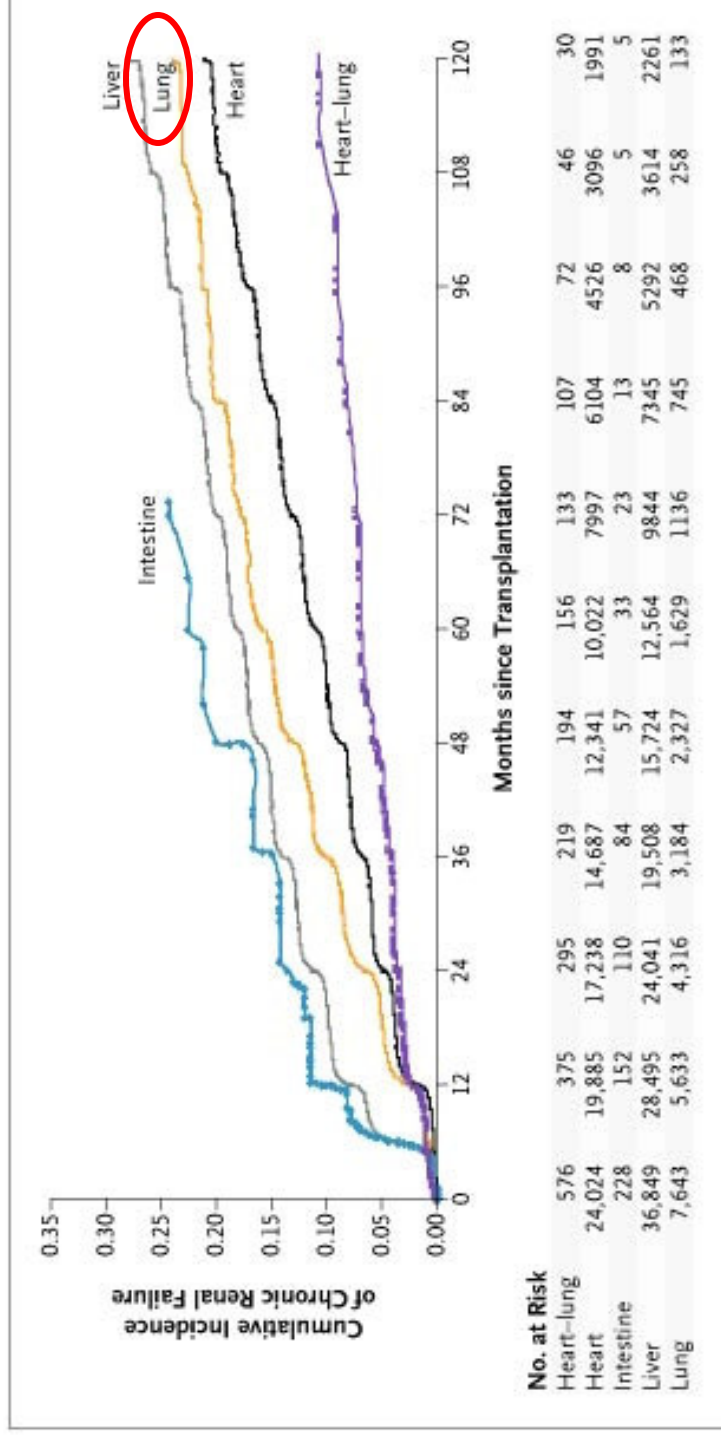
# Trasplante pulmonar Calcineurínicos si o no:

- ¿Deberían emplearse menos?





# INH's y toxicidad renal



OJO AO. New Engl J Med 2003;931-40

# POST-LUNG TRANSPLANT MORBIDITY FOR ADULTS

Cumulative Prevalence in Survivors within 1 and 5 Years  
 Post-Transplant (Follow-ups: April 1994 - June 2009)

<u>Outcome</u>	<u>Within 1 Year</u>	<u>Total number with known response</u>	<u>Within 5 Years</u>	<u>Total number with known response</u>
Hypertension	52.5%	(N = 11,797)	84.4%	(N = 3,271)
Renal Dysfunction	24.40%	(N = 12,732)	34.7%	(N = 3,834)
<i>Abnormal Creatinine &lt; 2.5 mg/dl</i>	16.8%		23.1%	
<i>Creatinine &gt; 2.5 mg/dl</i>	5.9%		8.3%	
<i>Chronic Dialysis</i>	1.6%		2.8%	
<i>Renal Transplant</i>	0.1%		0.5%	
Hyperlipidemia	24.2%	(N = 12,521)	56.5%	(N = 3,600)
Diabetes	26.3%	(N = 12,694)	38.0%	(N = 3,551)
Bronchiolitis Obliterans Syndrome	9.6%	(N = 11,997)	36.9%	(N = 2,965)



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# POST-LUNG TRANSPLANT MORBIDITY FOR ADULTS

Cumulative Prevalence in Survivors within 10 Years Post-Transplant (Follow-ups: April 1994 - June 2009)

<u>Outcome</u>	<u>Within 10 Years</u>	<u>Total number with known response</u>
Hypertension	97.3%	(N = 337)
Renal Dysfunction	41.5%	(N = 612)
<i>Abnormal Creatinine &lt; 2.5 mg/dl</i>	26.5%	
<i>Creatinine &gt; 2.5 mg/dl</i>	5.9%	
<i>Chronic Dialysis</i>	6.9%	
<i>Renal Transplant</i>	2.3%	
Hyperlipidemia	68.5%	(N = 410)
Diabetes	37.4%	(N = 374)
Bronchiolitis Obliterans Syndrome	54.1%	(N = 379)



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J Heart Lung Transplant. 2010 Oct; 29 (10): 1083-1141

# Trasplante pulmonar Calcineurínicos si o no:

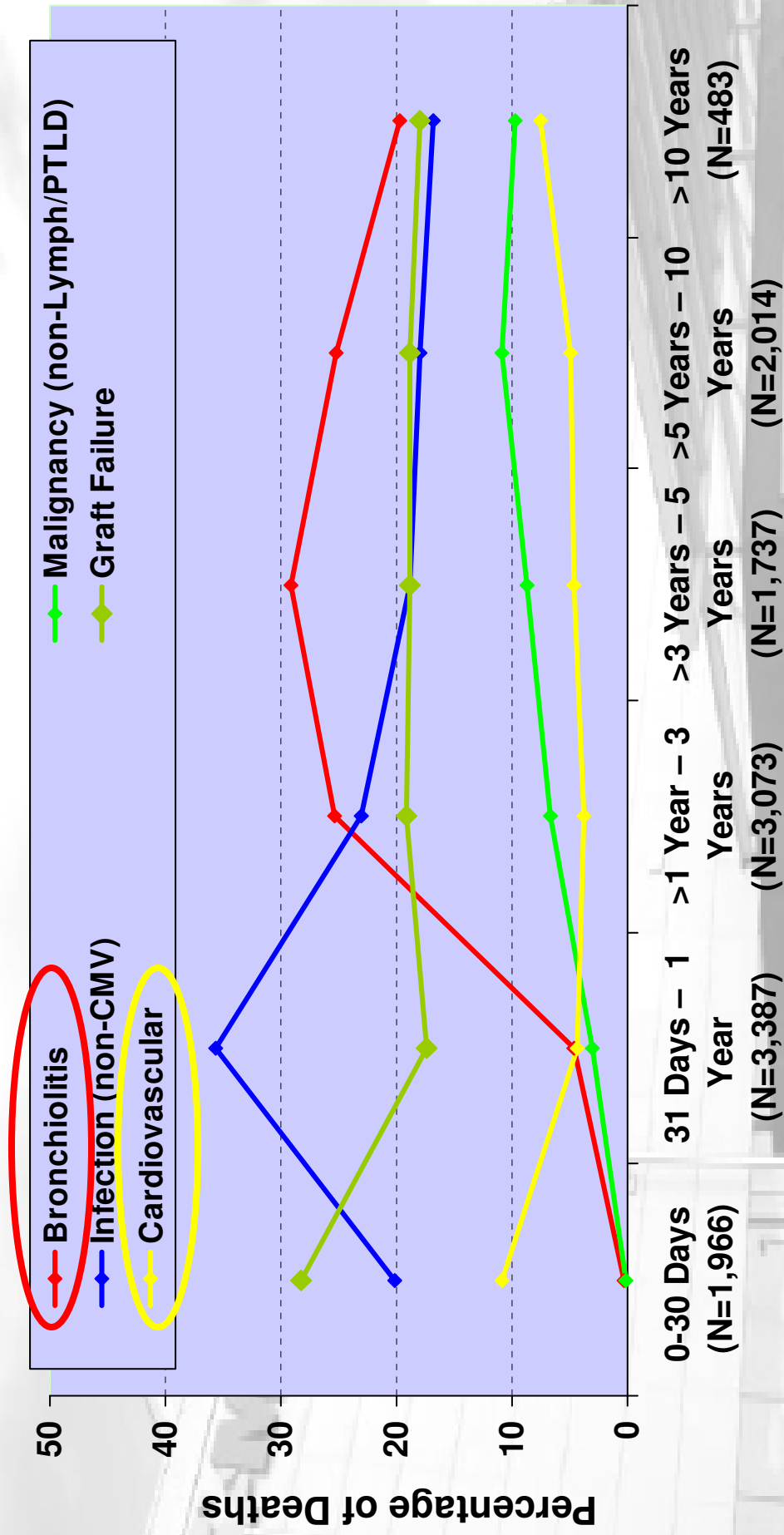


- ¿Por qué se siguen empleando?



# ADULT LUNG TRANSPLANT RECIPIENTS:

Relative Incidence of Leading Causes of Death  
(Deaths: January 1992 - June 2009)

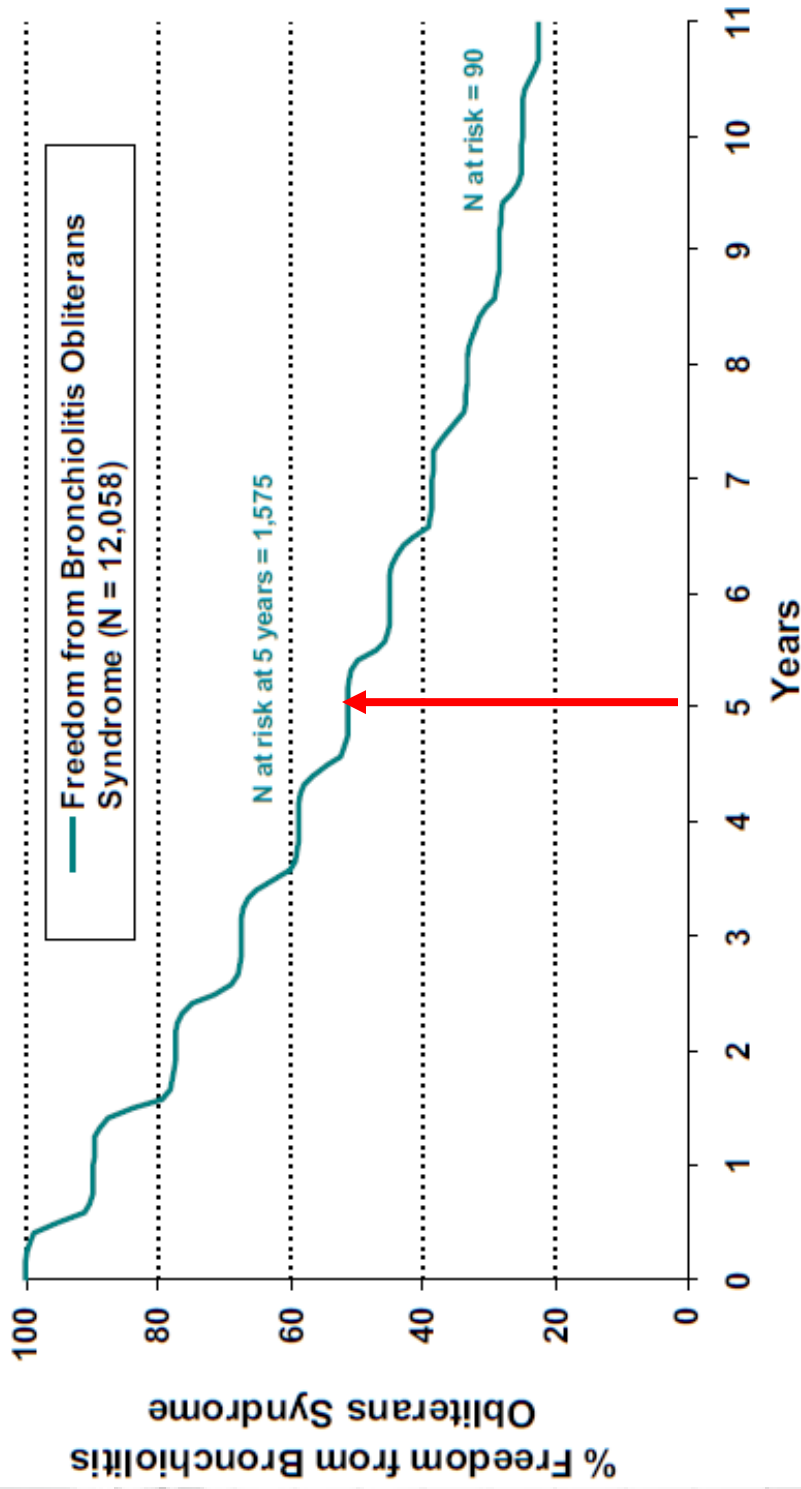


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# FREEDOM FROM BRONCHIOLITIS OBLITERANS SYNDROME

For Adult Lung Recipients (Follow-ups: April 1994-June 2009)  
Conditional on Survival to 14 days

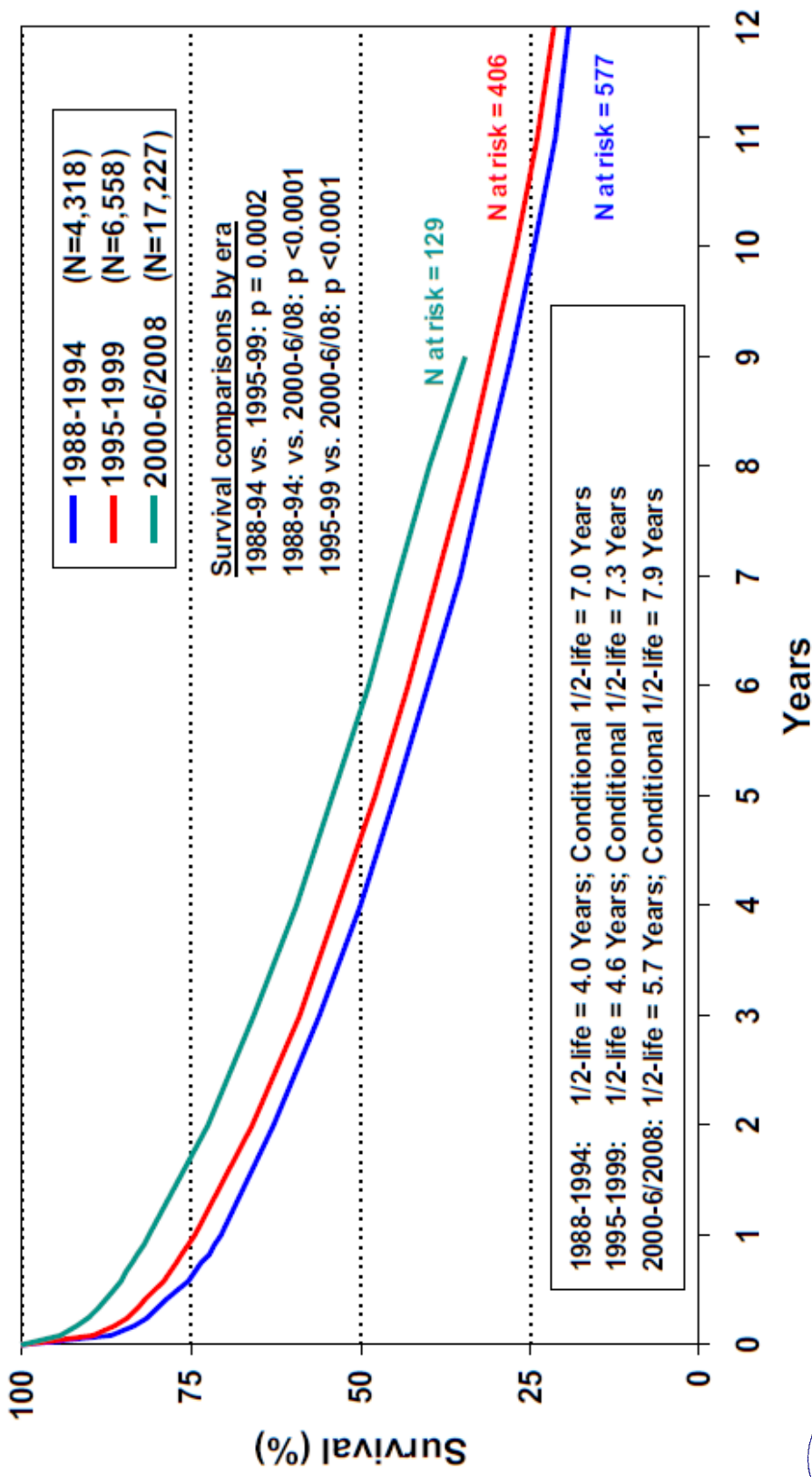


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# ADULT LUNG TRANSPLANTATION

Kaplan-Meier Survival by Era (Transplants: January 1988 – June 2008)

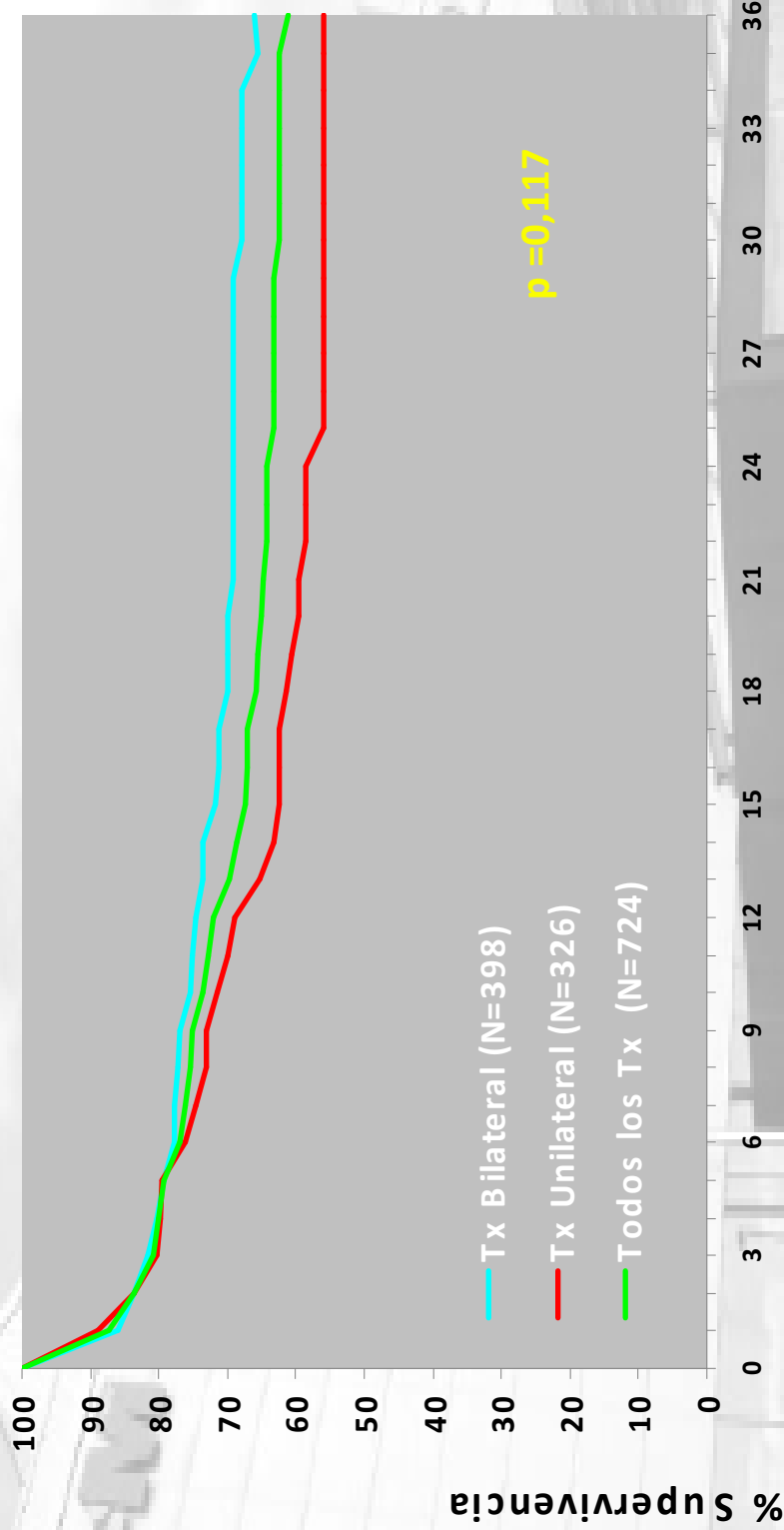


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# TRASPLANTE PULMONAR ADULTOS

Supervivencia Kaplan-Meier (Trasplantes: Enero 2006– Diciembre 2009)



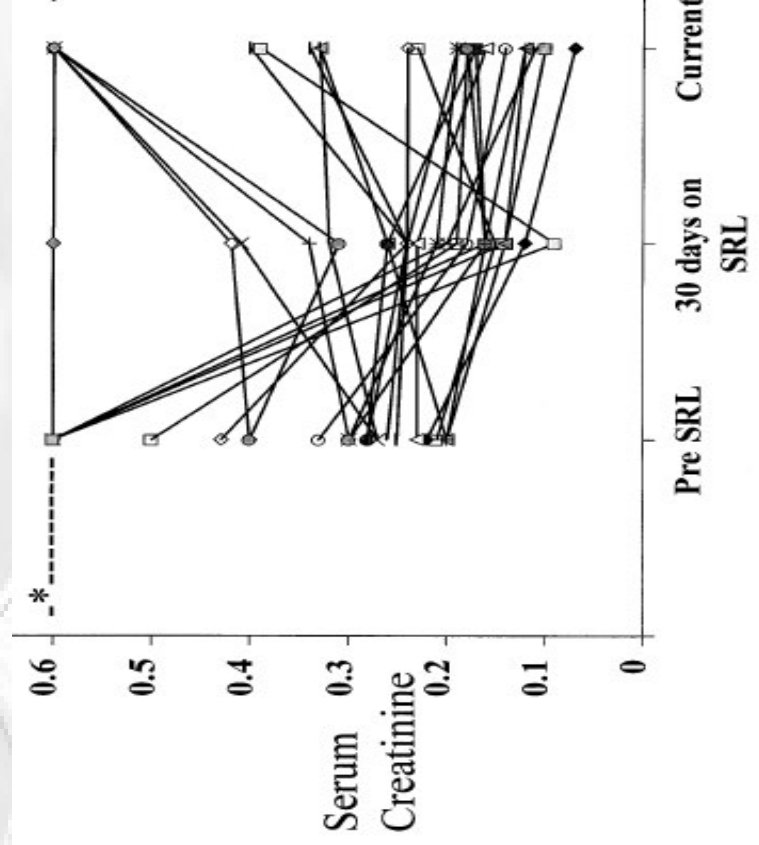


# Trasplante pulmonar Calcineurínicos si o no:

- ¿Existen alternativas?  
*Retirada completa*  
*Minimización*



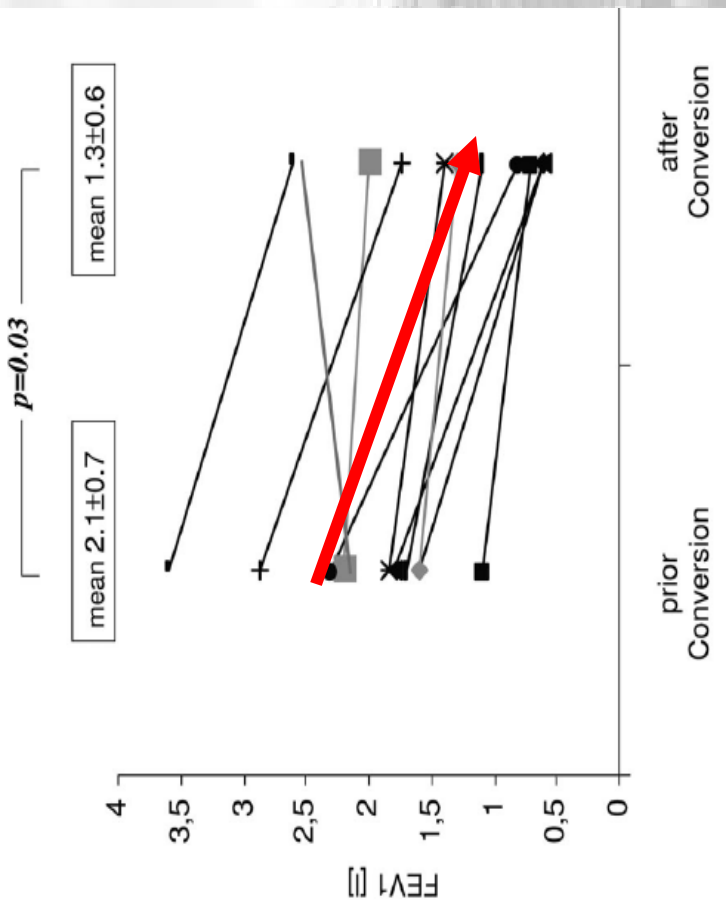
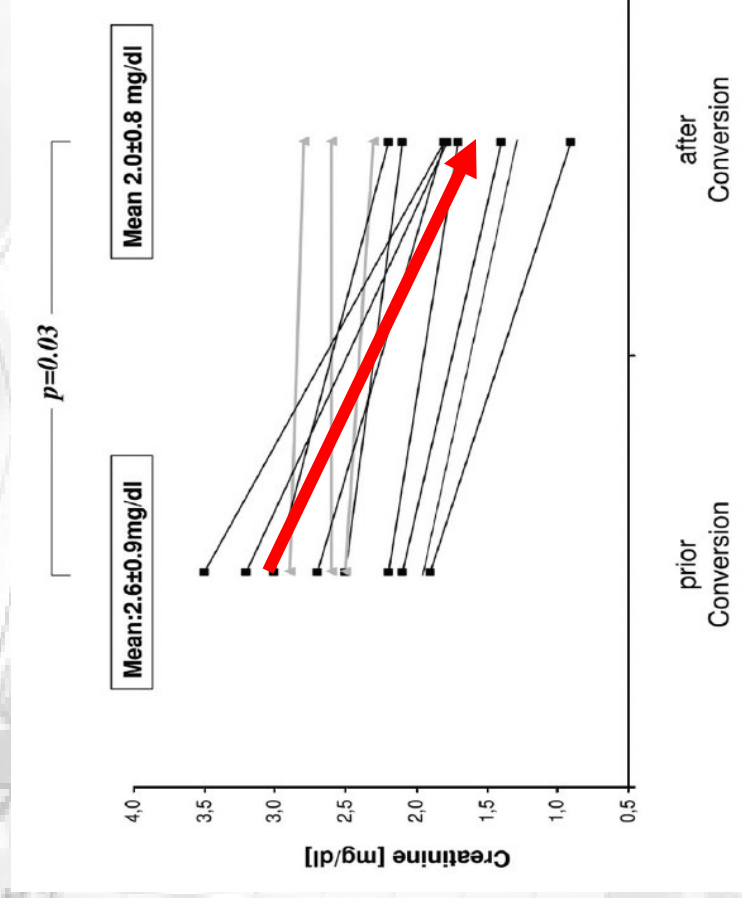
# RETIRADA DE INH: Sirolimus



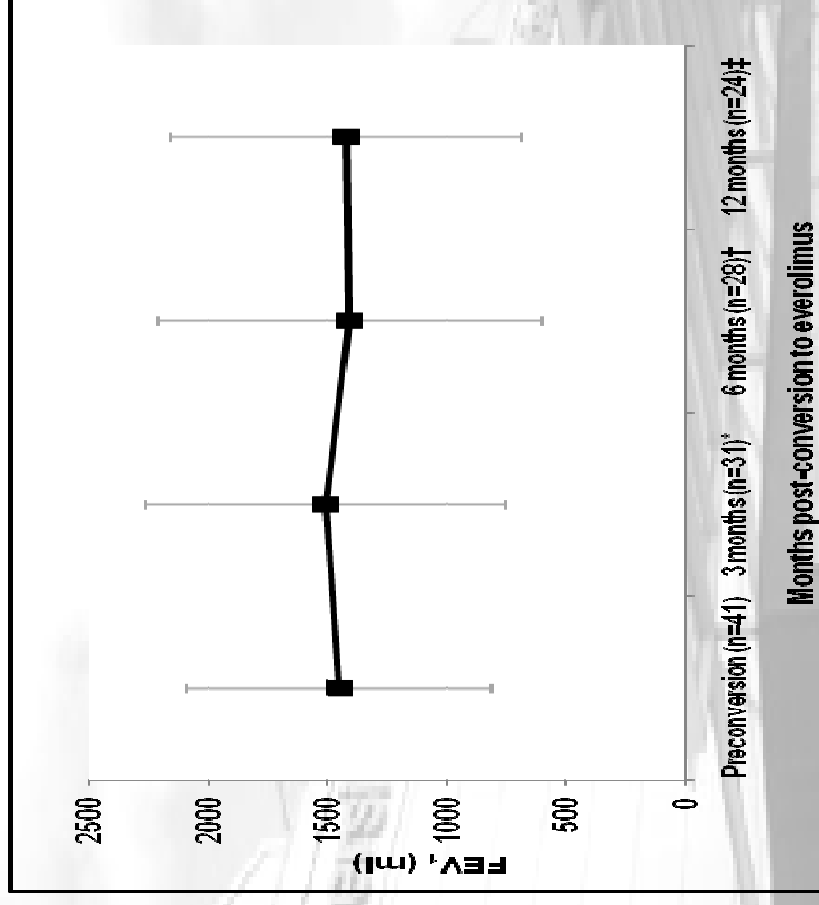
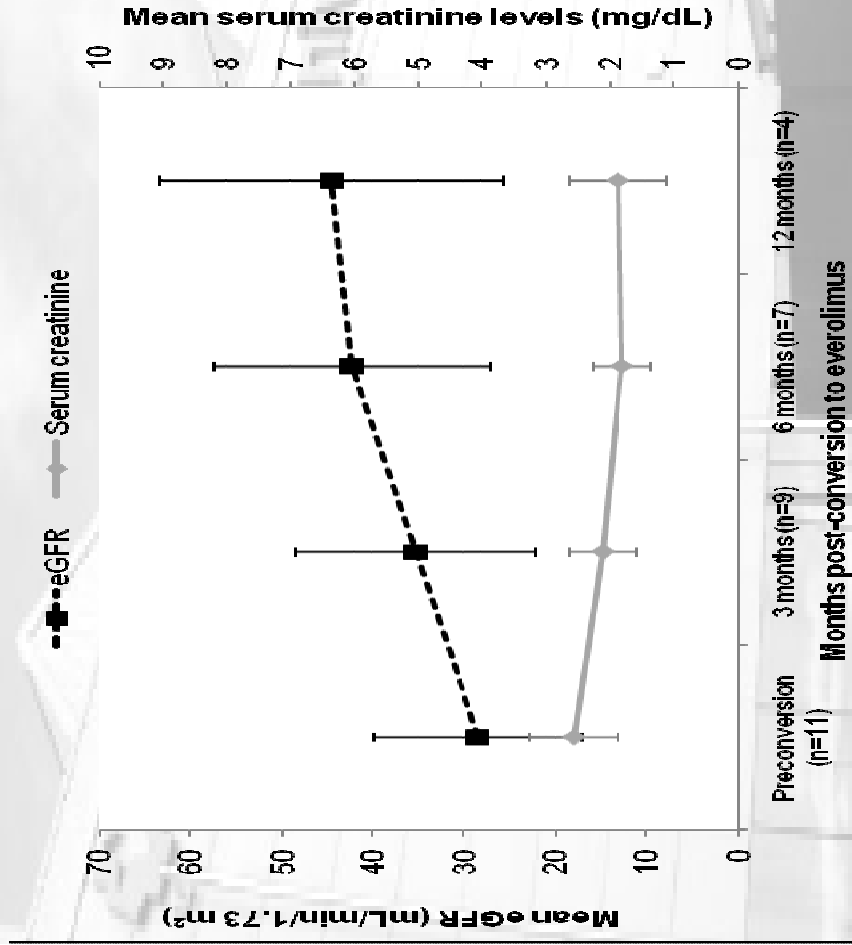
- 20 LTx con Insf. Renal Aguda
- Retirada del INH en el 48% y reducción del dosis
- 15 retirar la diálisis
- Eleveda toxicidad
  - 35 Infecciones
  - 2 RA
  - 24 toxicidad SRL
  - Retirada del fármaco
- Dosis altas sin ajuste de niveles

# RETIRADA DE INH: Sirolimus

11 LTx (5 CyA, 6 FK); SRL, 20 MMF, CS; 2 RA; Progresión de la BOS



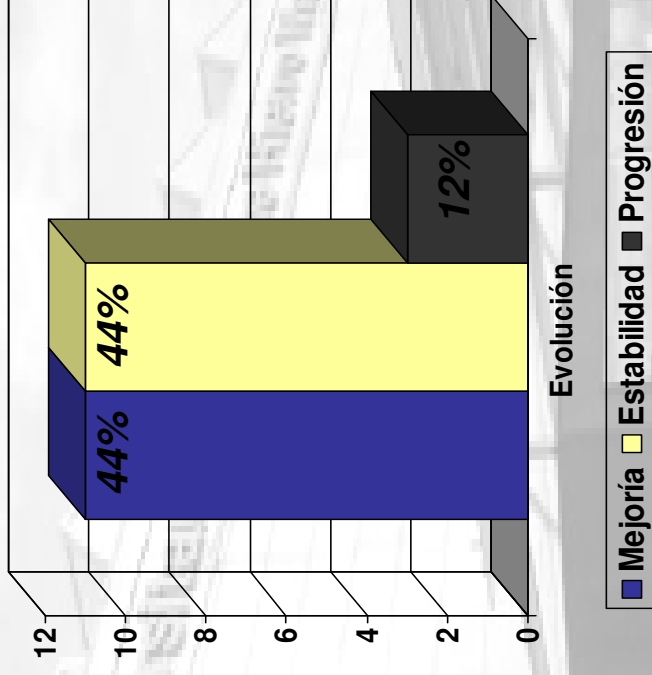
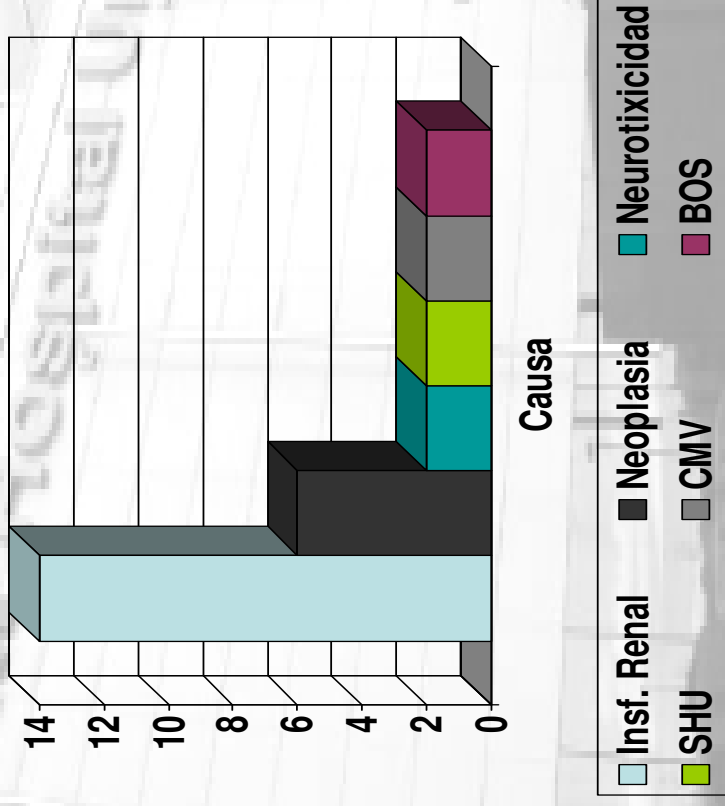
# RETIRADA DE INH: Everolimus



Roman A (EVERODATA). Transplan Proc 2011 (en prensa)

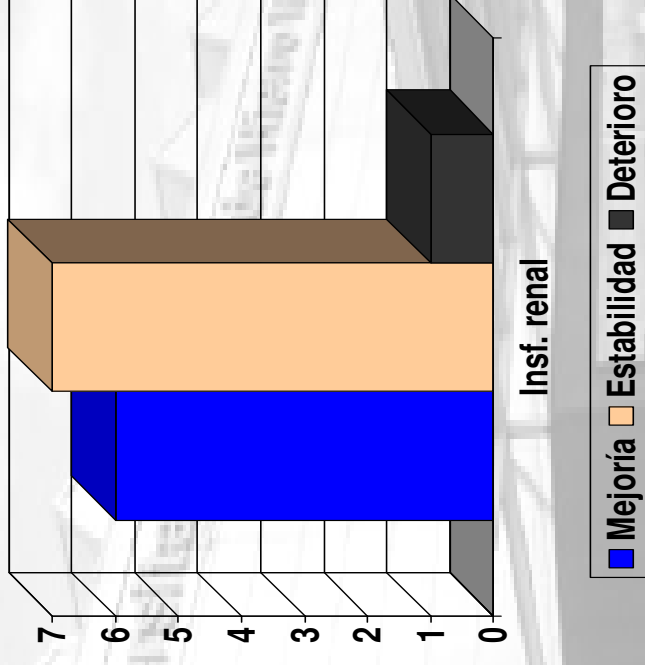
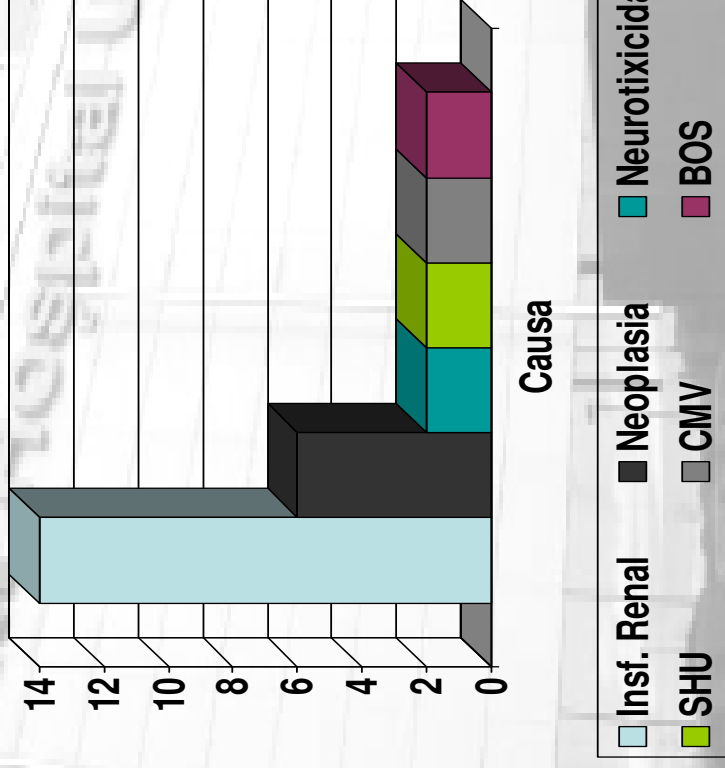
# RETIRADA DE INH: Experiencia Española

25 LTx (10 CyA, 14 FK); mTOR 24 (19 EVE, 6 SRL), 5 AZA y 20 MMF, CS  
Edad  $49 \pm 18$  años (12-71); Tiempo Post- trasplante:  $22 \pm 18$  meses (1-72)



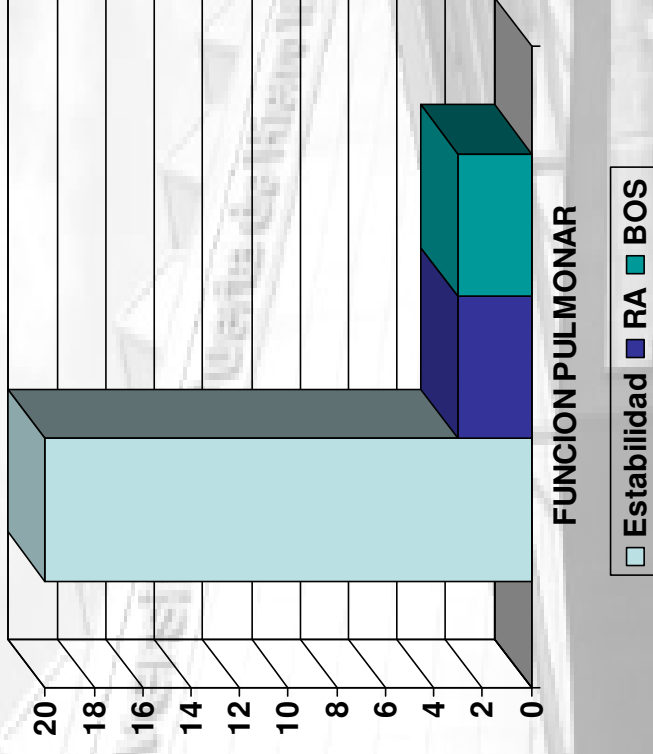
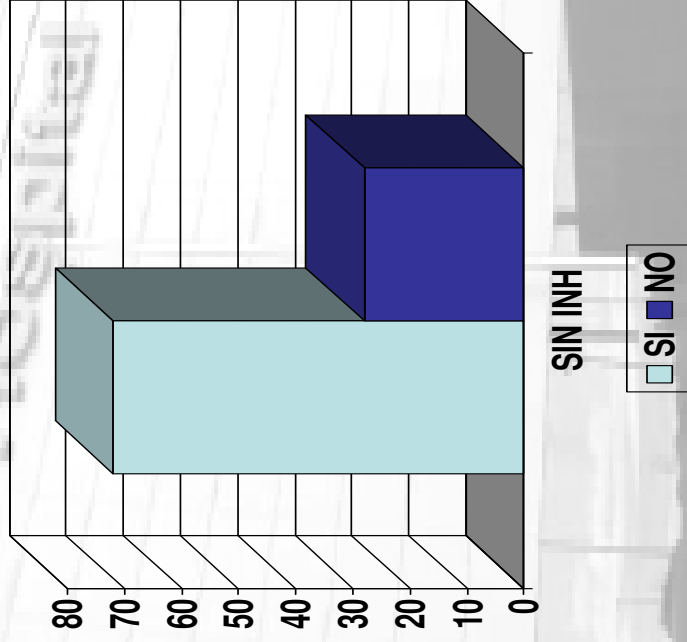
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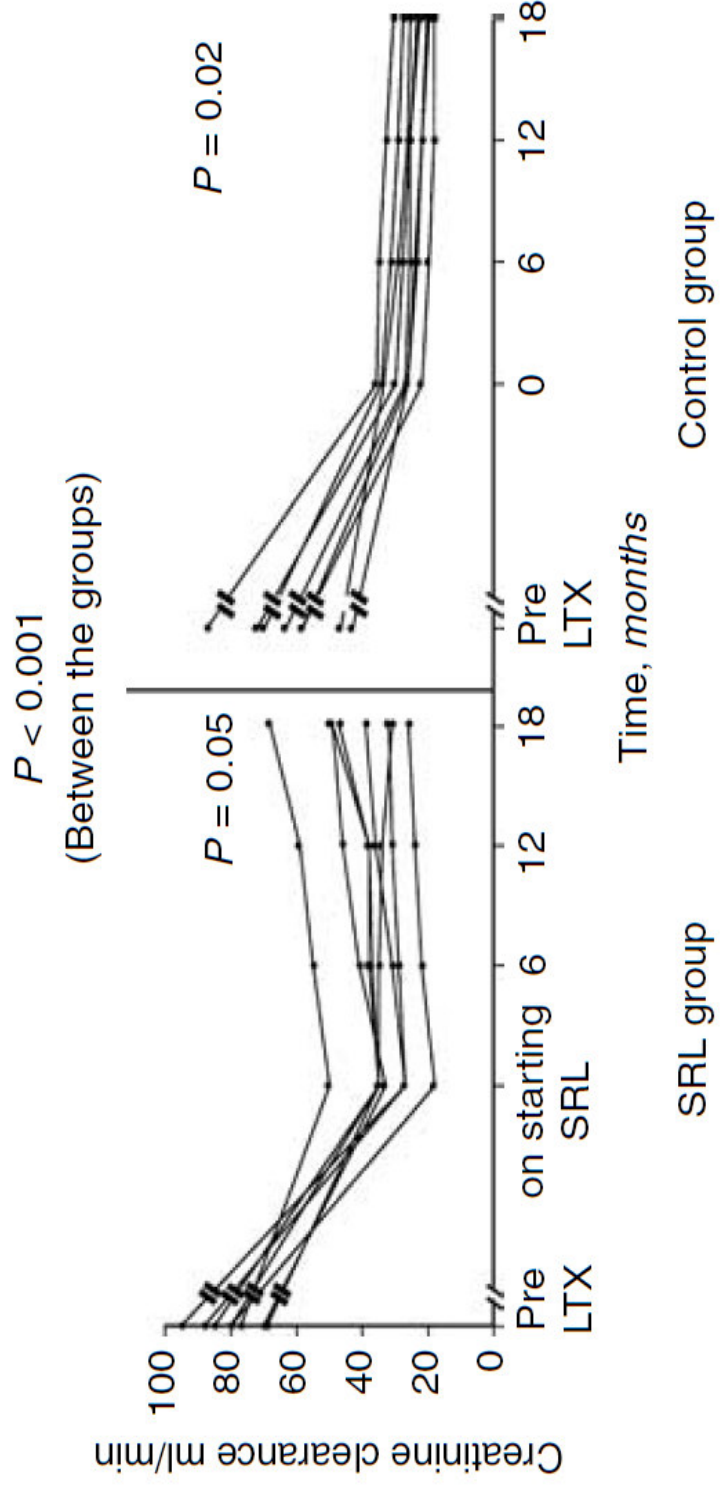
# RETIRADA DE INH: Experiencia Española

Seguimiento 22 ± 18 meses (1-72)



# DOSIS BAJAS INH: Sirolimus

- 16 LTx con FGR < 50 ml/min; Tiempo post-Tx 31 ± 1,2 meses
  - 8 SRL / INH (4-8 y 80-120 ng/mL)
  - 8 INH / AZA/Cs (estandar)





# DOSIS BAJAS INH: Everolimus

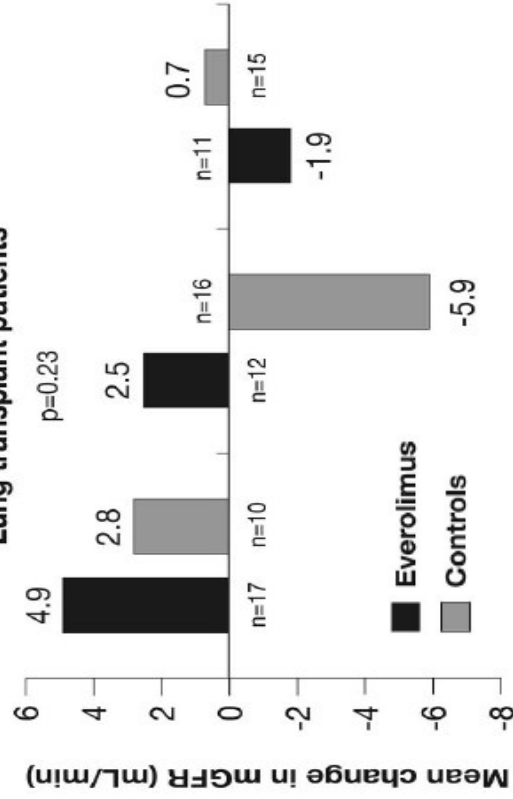
92 LTx con FGR<50ml/min

46 INH / AntM / CS vs. 46 EVE / Dosis bajas INH / AntM / CS

Tertile: 12-36 months 36-96 months >96 months

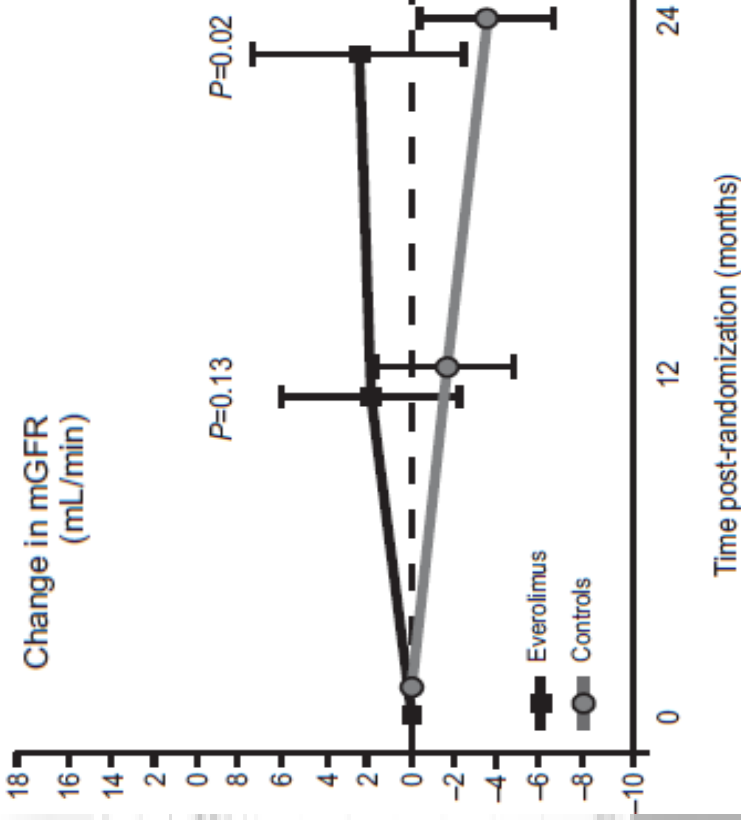
Time post-transplant

Lung transplant patients

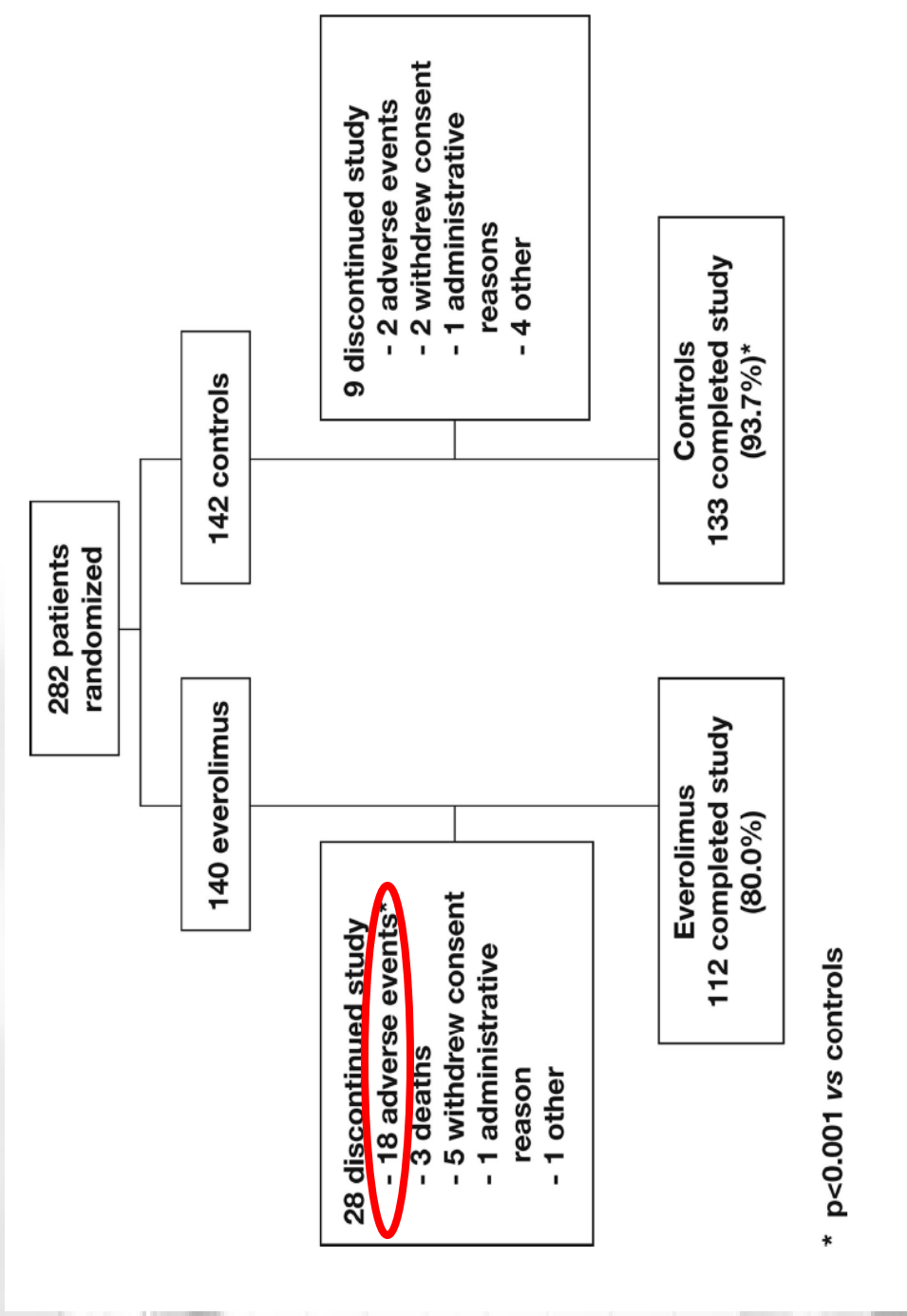


Tertile: 12-28 months 28-56 months >56 months

Time post-transplant



# DOSIS BAJAS INH: Everolimus



- Función Renal
- HTA
- Hiperlipidemia
- Diabetes
- CMV
- Tumores ?

- Rechazo Agudo
- BOS
- Mortalidad Cardiovascular

# Resumen y conclusiones:

- *La retirada de INH's es posible en algunos receptores de trasplante pulmonar.*
- *La retirada o reducción precoz de INH's se acompaña de mejoría de la función renal.*
- *Está por definir el momento optimo para su supresión y el perfil del paciente de bajo riesgo inmunológico.*
- *Los protocolos de minimización de INH's en combinación con los PSI presentan un mejor perfil de toxicidad renal sin mayor riesgo de rechazo pulmonar.*

