

# **Manejo de las alteraciones óseo-metabólicas en el trasplante renal**

**JV Torregrosa  
Hospital Clínic. Barcelona**

**4º Congreso de la Sociedad Gallega de Nefrología  
Lugo, noviembre 2017**

- **Mujer de 59 años que va a recibir un segundo trasplante renal de donante en muerte encefálica**
- **Antecedentes médicos relevantes:**
  - LES a los 21 años. Recibió altas dosis esteroides
  - HD a los 39 años
  - A los 41 años, recibió TR donante muerte encefálica
  - Regreso a HD a los 56 años (Rechazo crónico)
  - PRA >50%
  - Amenorrea

- **Medicación en diálisis:**
  - Captores de fósforo (Ac. cálcico 500 mg/2 al dia y Sevelamer 800 mg en cada comida)
  - Cinacalcet 60 mg/dia
- **En el momento del trasplante:**
  - PTHi: 370 pg/ml
  - Ca: 9.1 mg/dL
  - P: 5.1 mg/dL
  - Fosfatasas alcalinas: 314 IU/L
  - 25(OH)D: 35 ng/ml
- **Immunosupresion de inducción:**
  - Timoglobulina, Tacrolimus, MMF and Steroids

## A los 10 días del TR

- **Clinicamente bien**
- **Analítica sanguínea:**
  - Creatinina: 1.5 mg/dL
  - Ca: 10.4 mg/dL
  - P: 1.9 mg/dL
  - **Fosfatasas alcalinas: 371 UI/L**
- **Rx dorso-lumbar:**  
**No fracturas**
- **DEXA**
  - **T-score columna lumbar: -2**
  - **T-score cuello femoral: -1,8**
  - **T-score radio: -1,9**



## **Alteraciones óseo-metabólicas más frecuentes post TR:**

- **Hipercalcemia**
- **Hipofosfatemia**
- **Pérdida de masa ósea. Fracturas**

## ¿ Cómo esta la Calcemia post TR ?

### Evolución del balance mineral en los 3 m postrasplante

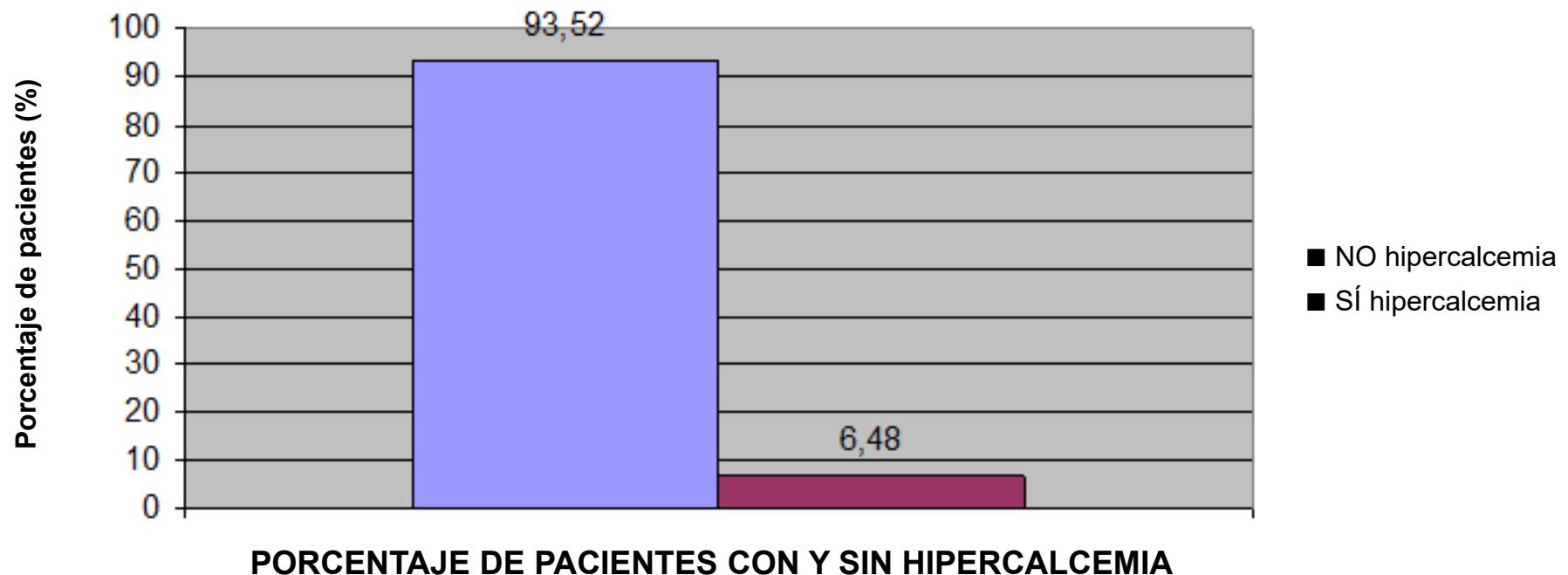
Table 3. Parameters of mineral metabolism at the time of transplantation and at 3 mo<sup>a</sup>

| Parameter   | Transplantation | 3 Mo          | P       |
|---|-----------------|---------------|---------|
| PO <sub>4</sub> (mg/dl)                           | 4.8 ± 1.2       | 2.7 ± 0.7     | <0.0001 |
| Albumin (g/dl)                                    | 44.1 ± 5.3      | 43.1 ± 3.7    | 0.0100  |
| Ca (mg/dl)  | 9.59 ± 0.70     | 9.69 ± 0.59   | 0.0100  |
| Ca below/on/above K/DOQI targets (%)              | 9.0/41.8/49.3   | 1.0/85.6/13.4 | <0.0001 |
| Ca <sub>c</sub> (mg/dl)                           | 9.29 ± 0.80     | 9.44 ± 0.57   | <0.0001 |
| Ca <sub>c</sub> below/on/above K/DOQI targets (%) | 11.4/53.2/35.3  | 7.0/86.1/7.0  | <0.0001 |
| hypercalcemia (>10.3 mg/dl; %)                    | 9.0             | 7.0           | 0.4600  |

n: 201

## ¿ Cómo esta la Calcemia post TR ?

7 % de pacientes con Ca corregido >10,3 mg/dl



Torres A, Torregrosa JV, et al. Nefrologia 2016;36:255-67.

JV Torregrosa. Hospital Clinic. Barcelona

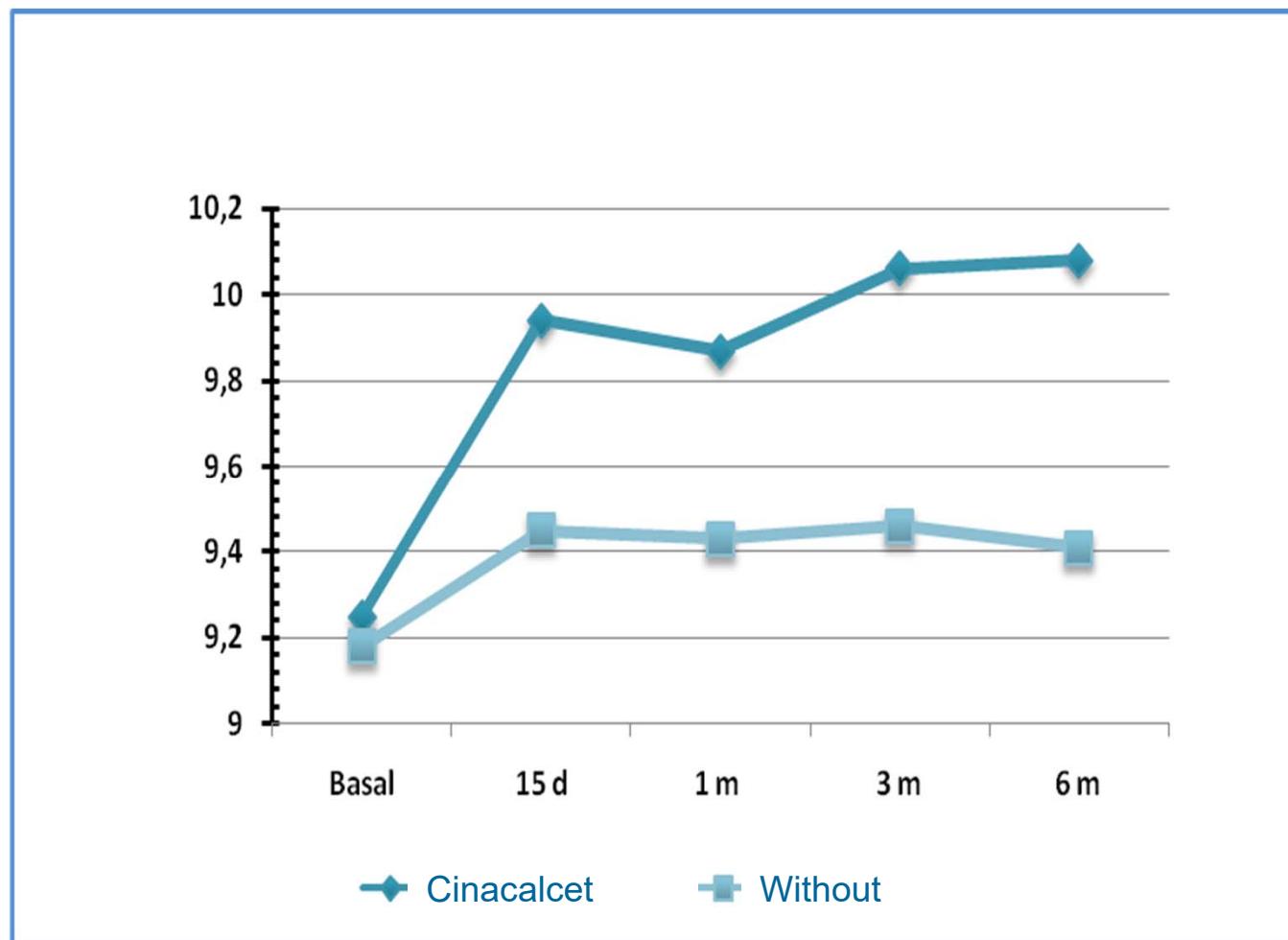
## ¿ Porqué se produce la hiperCalcemia post TR ?

### Factores asociados con la hiperCa post TR

| Independent Variables                | $\beta$ Coefficient | SE    | t    | p       | R <sup>2</sup> |
|--------------------------------------|---------------------|-------|------|---------|----------------|
| Univariate models                    |                     |       |      |         |                |
| serum $Ca_{c\text{ pre}}$            | 0.340               | 0.044 | 7.60 | <0.0001 | 0.230          |
| Ln PTH <sub>pre</sub>                | 0.180               | 0.042 | 4.20 | <0.0001 | 0.081          |
| serum PO <sub>4</sub> <sup>pre</sup> | 0.076               | 0.034 | 2.25 | 0.0260  | 0.025          |
| Multivariate model                   |                     |       |      |         |                |
| serum $Ca_{c\text{ pre}}$            | 0.400               | 0.040 | 9.45 | <0.0001 | 0.370          |
| PTH pre RT                           | 0.220               | 0.350 | 6.24 | <0.0001 |                |

## ¿ Porqué se produce la hiperCalcemia post TR ?

Cinacalcet pre-TR mayor incidencia de hiperCa postTR

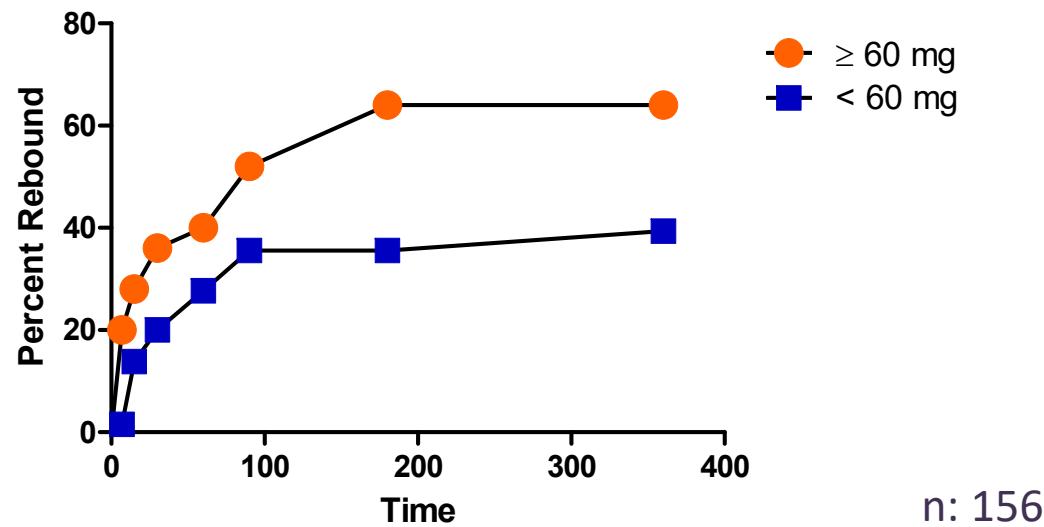


Barros X, Torregrosa JV. Transplantation 2012;94:

9

## ¿ Porqué se produce la hiperCalcemia post TR ?

A mayor dosis Cinacalcet pre-TR, mayor hiperCa postTR

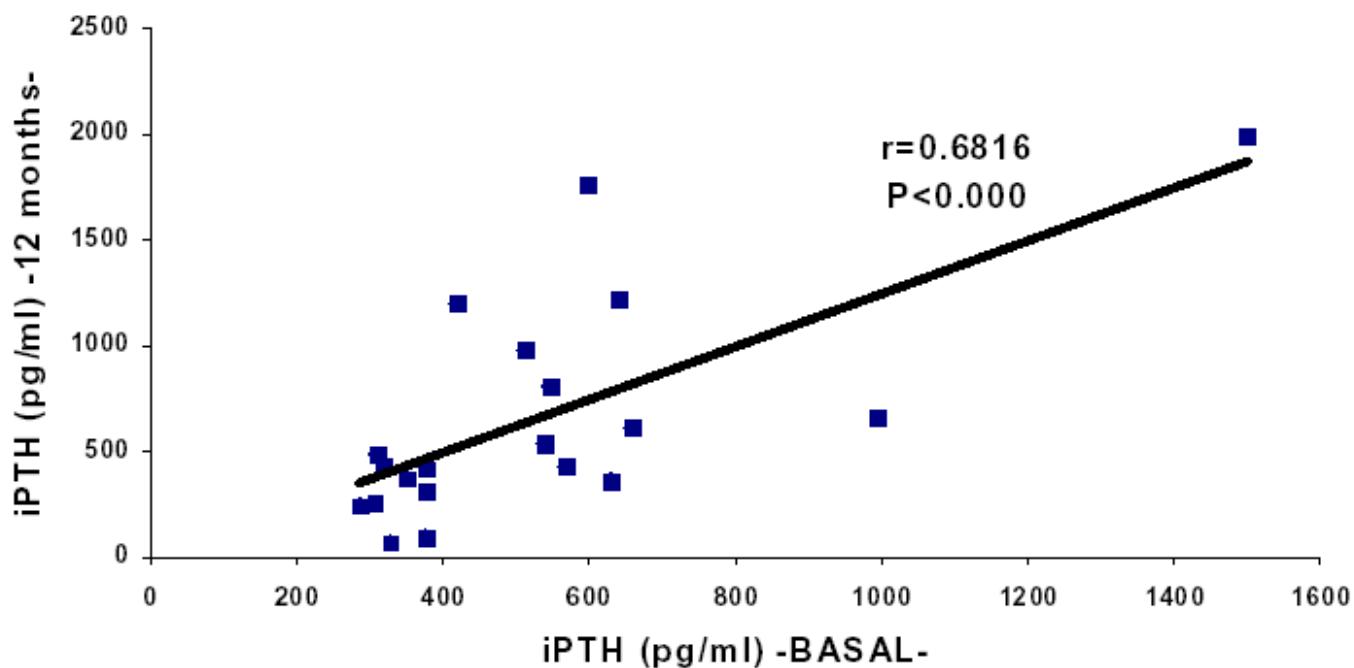


Torregrosa JV, et al. Transp Proc 2009;41:2396-8.

JV Torregrosa. Hospital Clinic. Barcelona

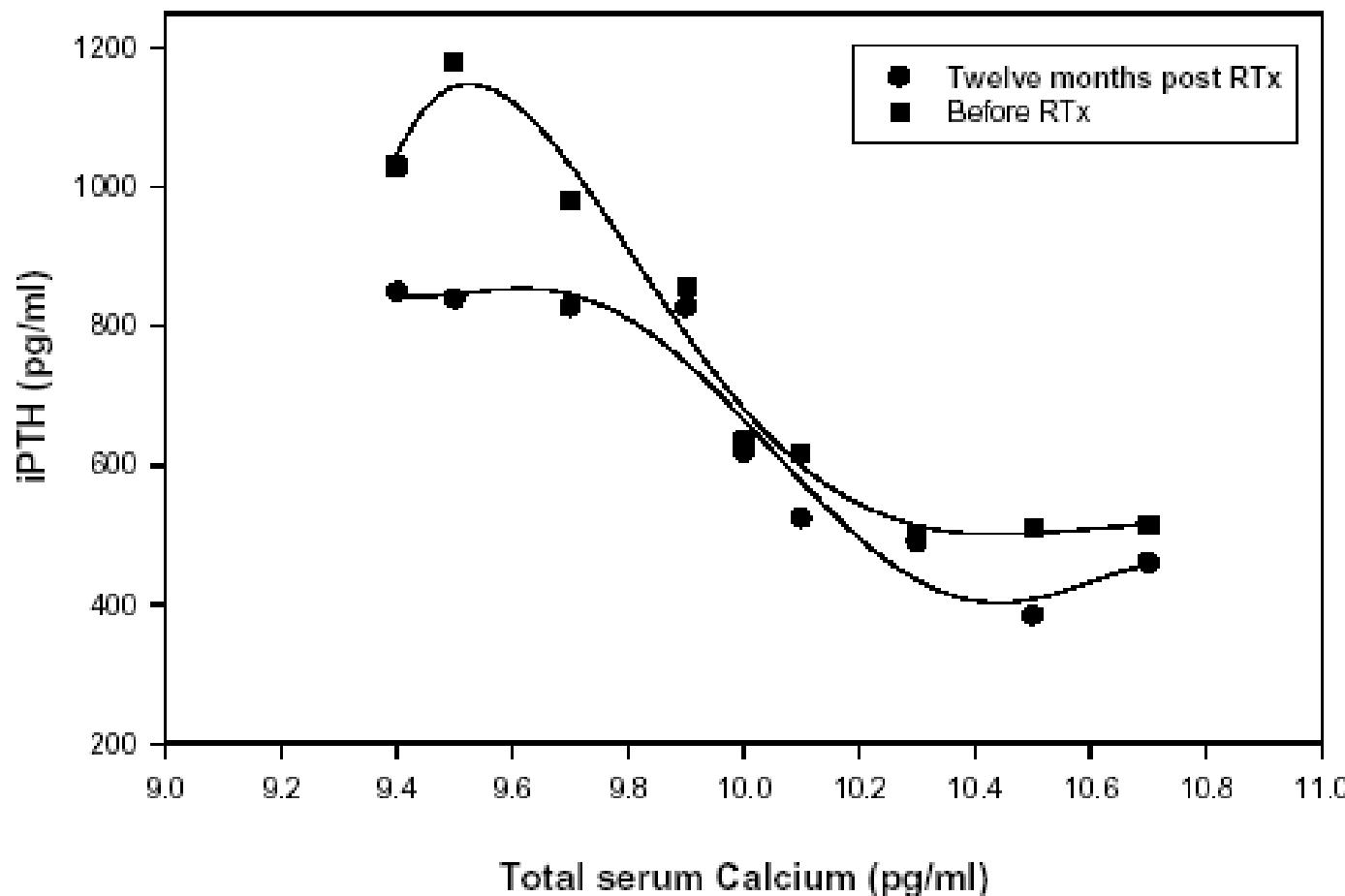
¿ Persiste ?

## PTHi POST-TRASPLANTE RENAL (según PTHi pre-TR)



¿ Persiste ?

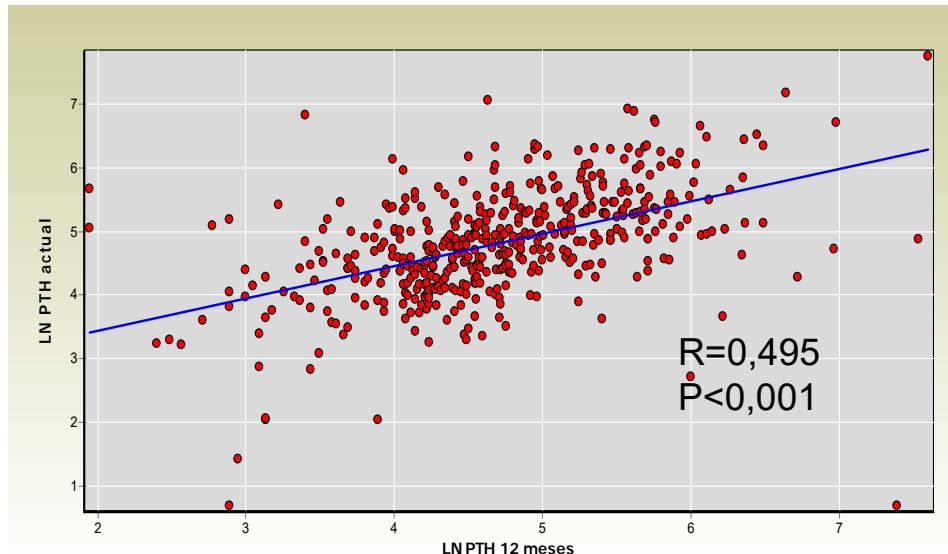
## Variación set-point de Ca



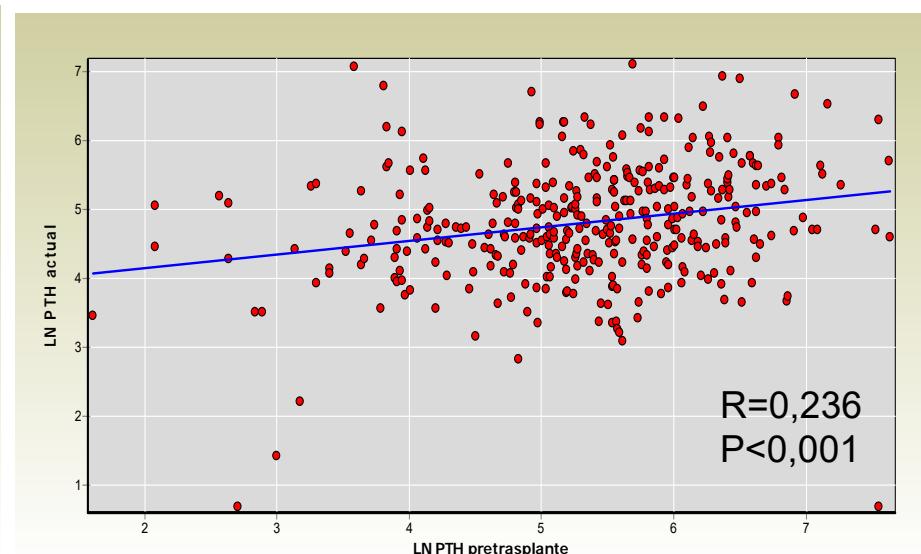
¿ Persiste ?

## PTHi a los 12 meses del trasplante y en pre-trasplante con la PTH actual

PTH a los 12 meses se correlaciona con PTH actual



PTH en el pre-trasplante se correlaciona con PTH actual



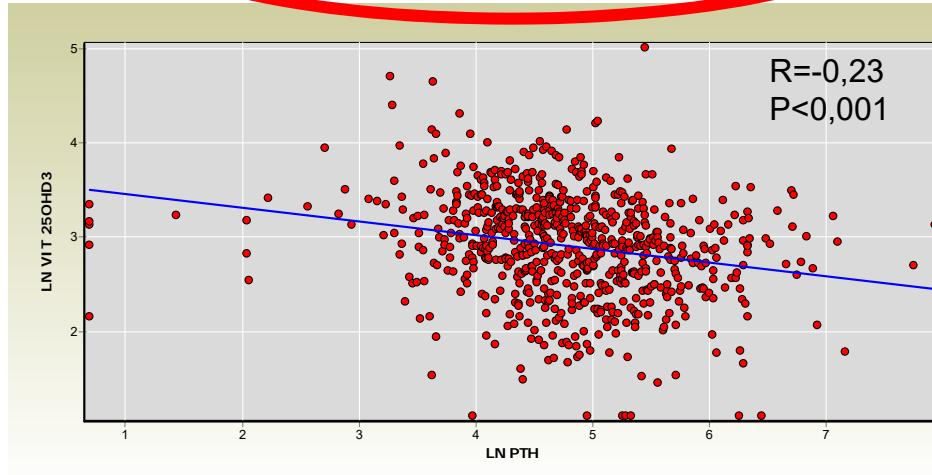
Torres A, Torregrosa JV, et al. Nefrologia 2016;36:255-67

JV Torregrosa. Hospital Clinic. Barcelona

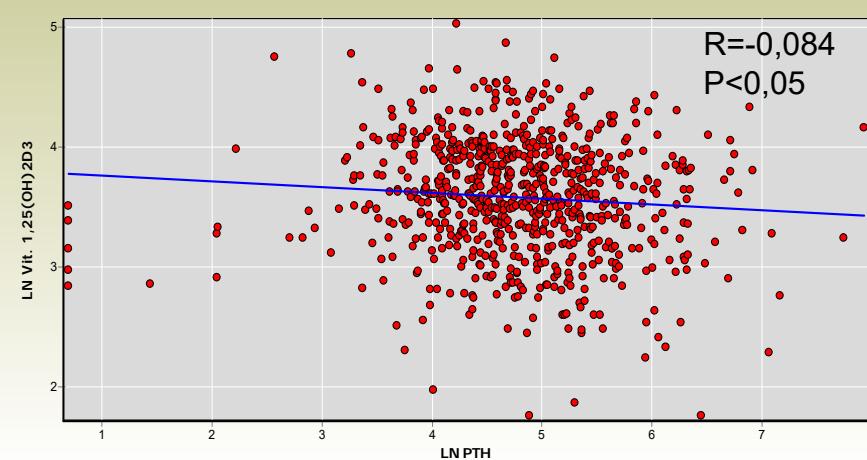
¿ Persiste ?

## Correlación inversa entre Vitamina D (25OHD3 y 1,25OH2D3) y PTH

Correlación entre niveles de PTH y  
25 (OH) Vit. D



Correlación entre niveles de PTH y  
de 1,25 (OH) Vit. D



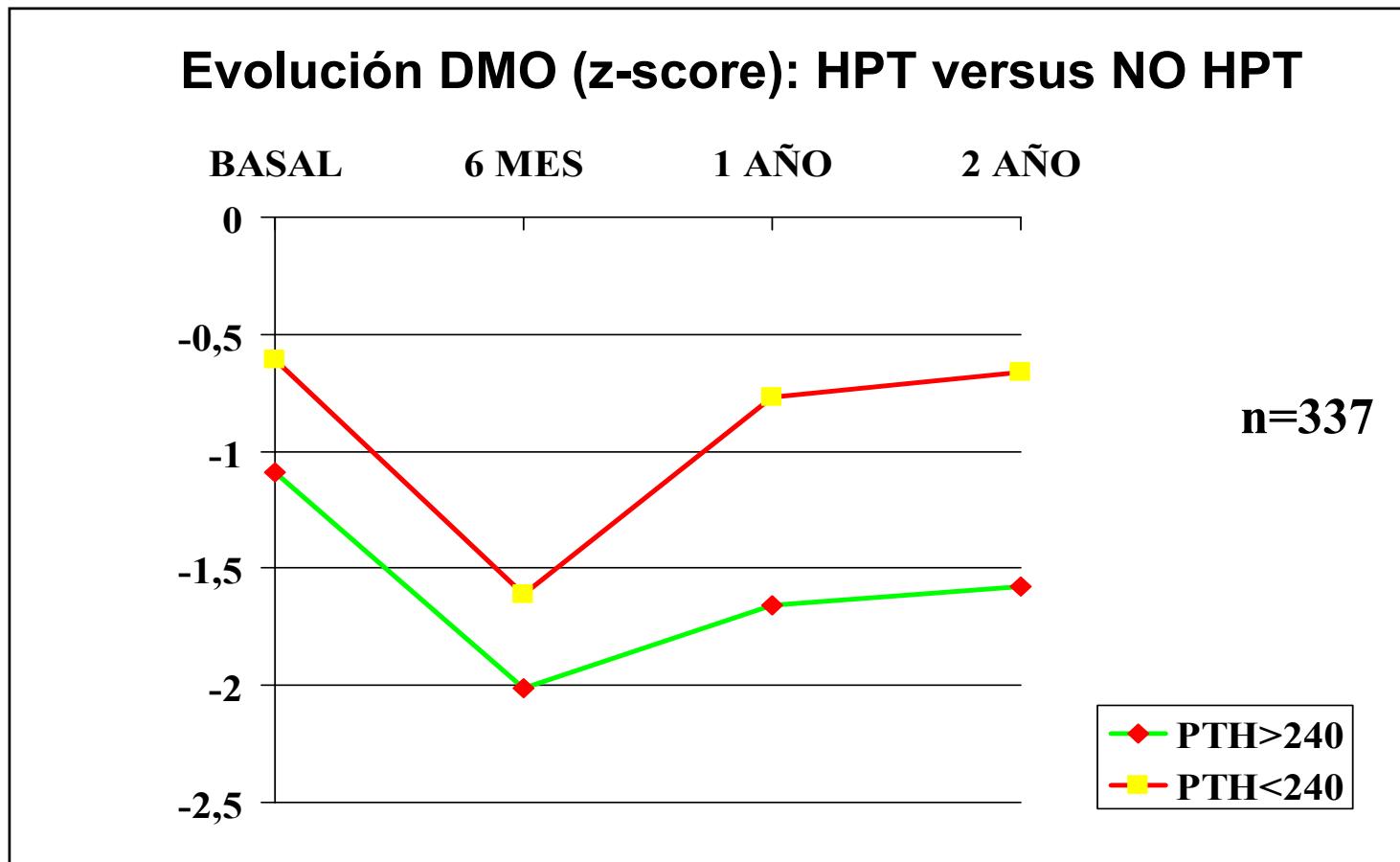
Torres A, Torregrosa JV, et al. Nefrologia 2016;36:255-67

JV Torregrosa. Hospital Clinic. Barcelona

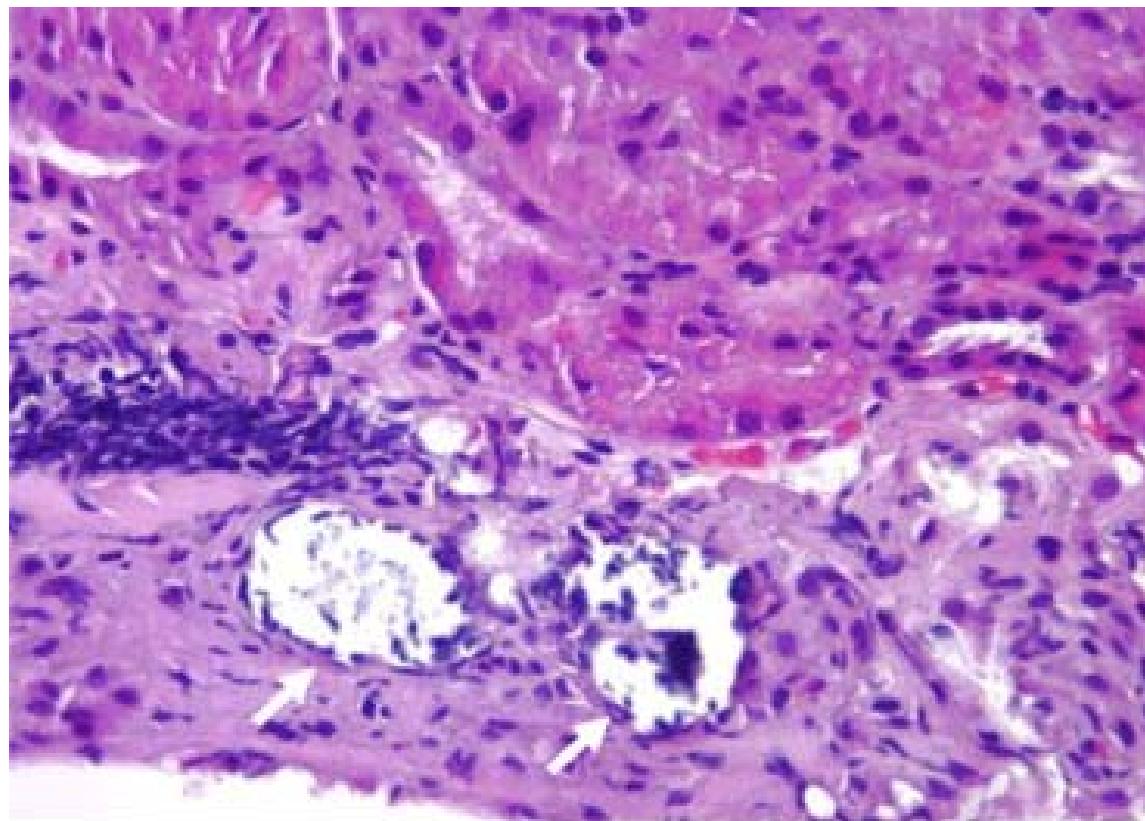


## Consecuencias

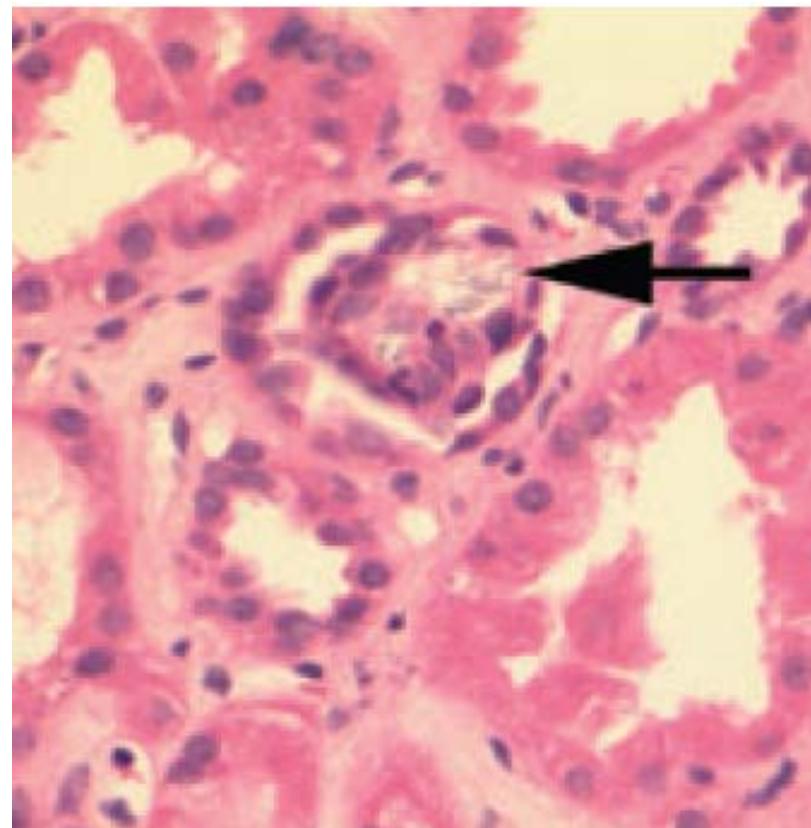
## Descenso persistente de la DMO



## Calcificaciones túbulo-intersticiales



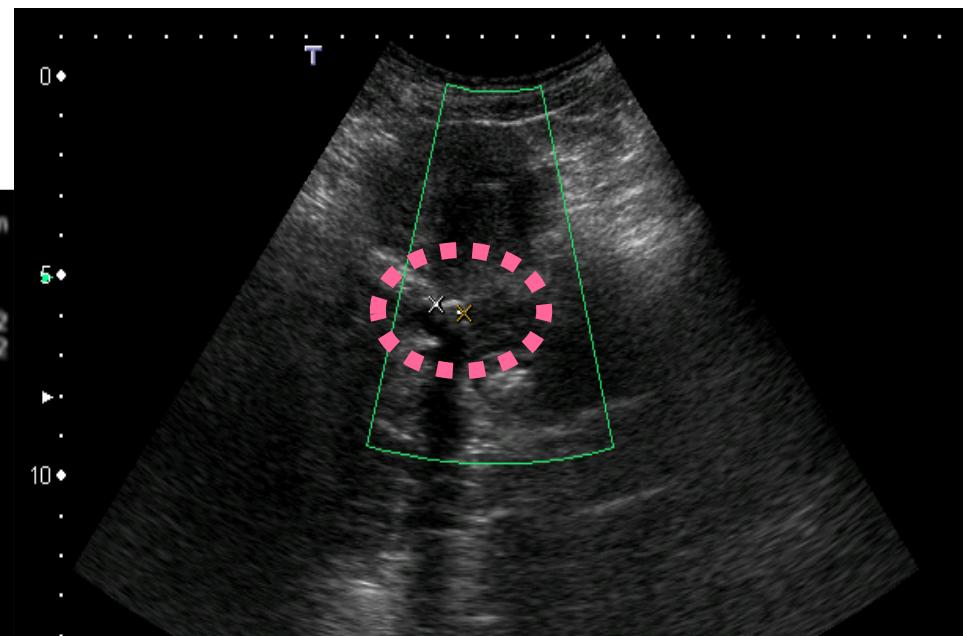
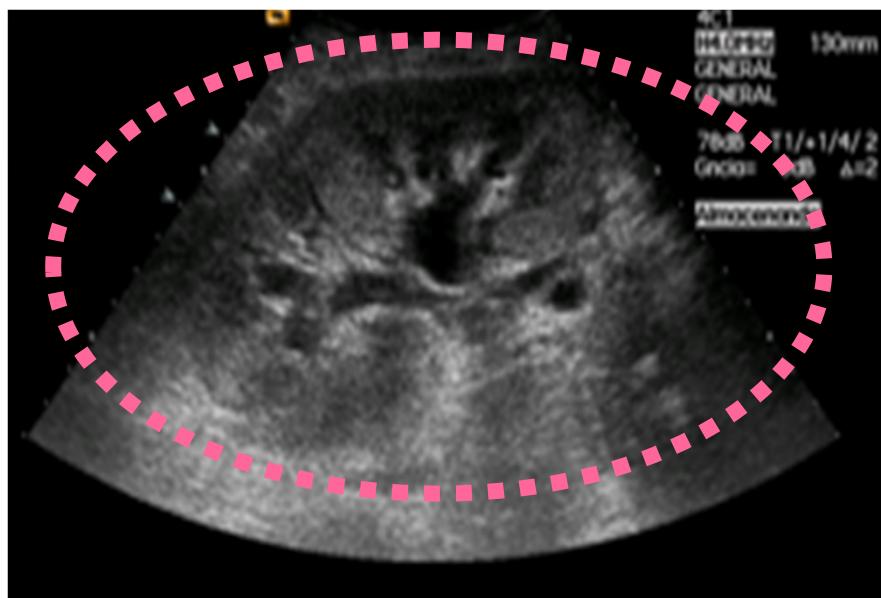
## Calcificaciones túbulo-intersticiales



Calcificación tubular (HE x400)<sup>1</sup>

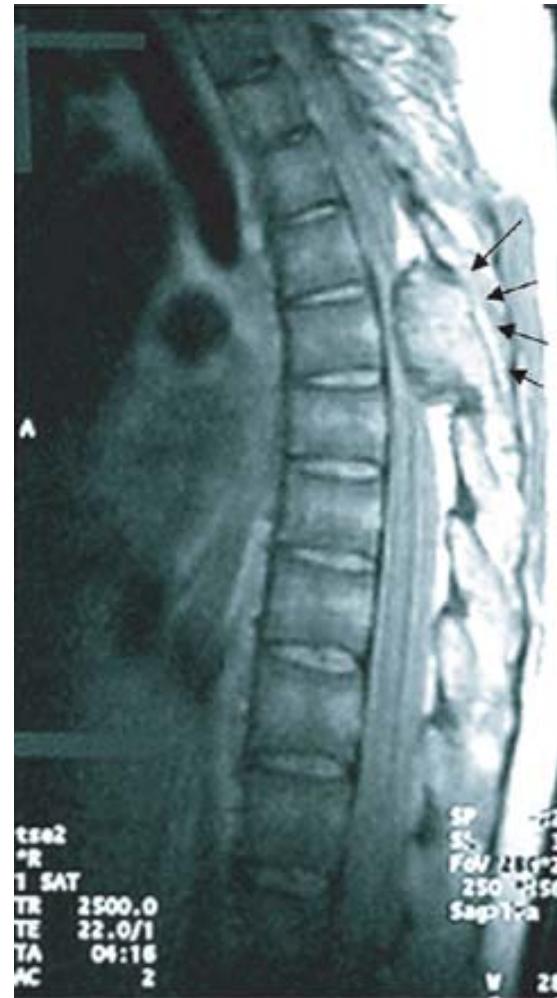
Personal data

# Calcificación ureteral



Personal data

## Brown tumor



Fuster D, Monegal A, Torregrosa JV. Kidney Int 2006;70:1533

JV Torregrosa. Hospital Clinic. Barcelona

## Posibilidades de manejo de la hiperCa post TR

- Conducta expectante
- Calcimiméticos (Cinacalcet)
- Paratiroidectomia

## Conducta expectante, excepto:

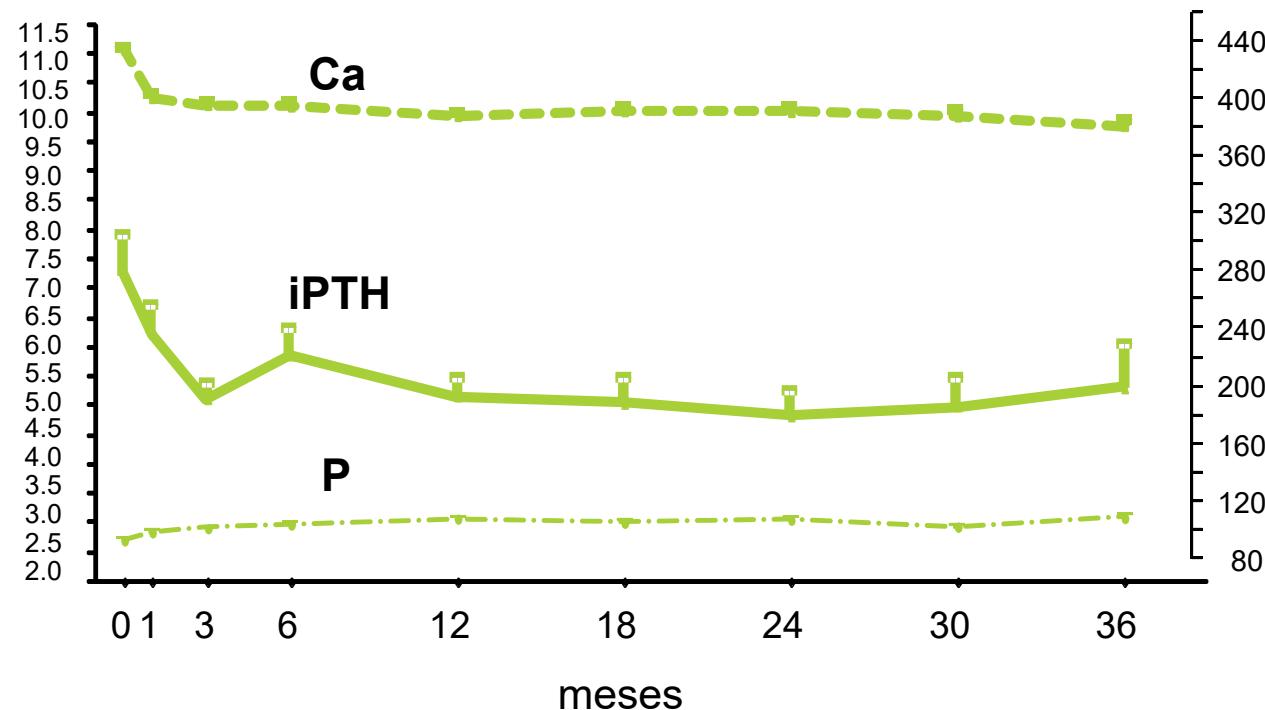
- HiperCa > 11 mg/dL
- HiperCa > 10,5 mg/dL más de 6 meses
- HiperCa sintomática

## Posibilidades de manejo de la hiperCa post TR

- Conducta expectante
- Calcimiméticos (Cinacalcet)
- Paratiroidectomia

## Cinacalcet controla hiperCa

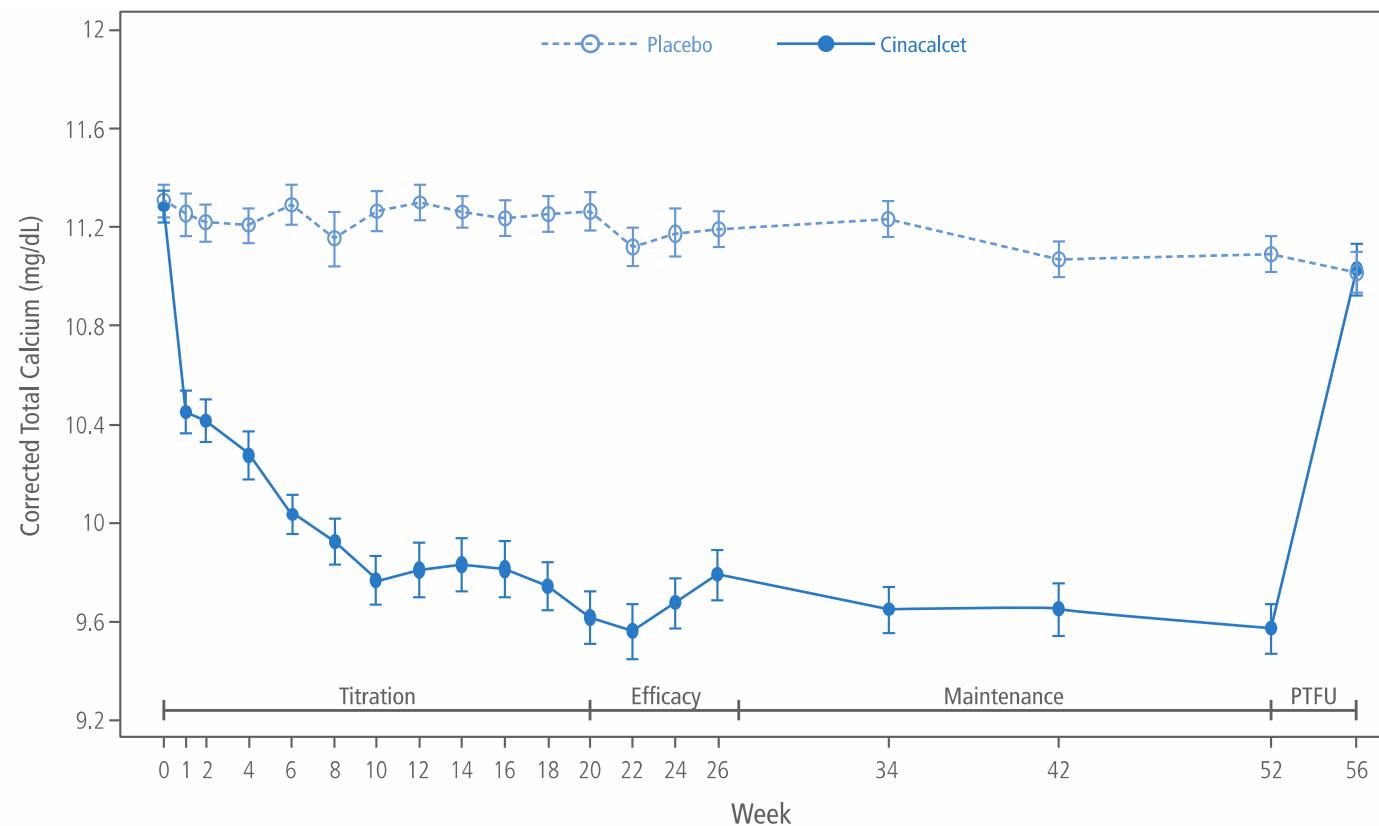
### Evolución Ca/P/iPTH



|      | % change at 6 months | Valor p |
|------|----------------------|---------|
| Ca   | 11,1-10,1<br>9,0%    | <0,0001 |
| iPTH | -23,0%               | 0,0005  |
| P    | 11,1%                | <0,0001 |

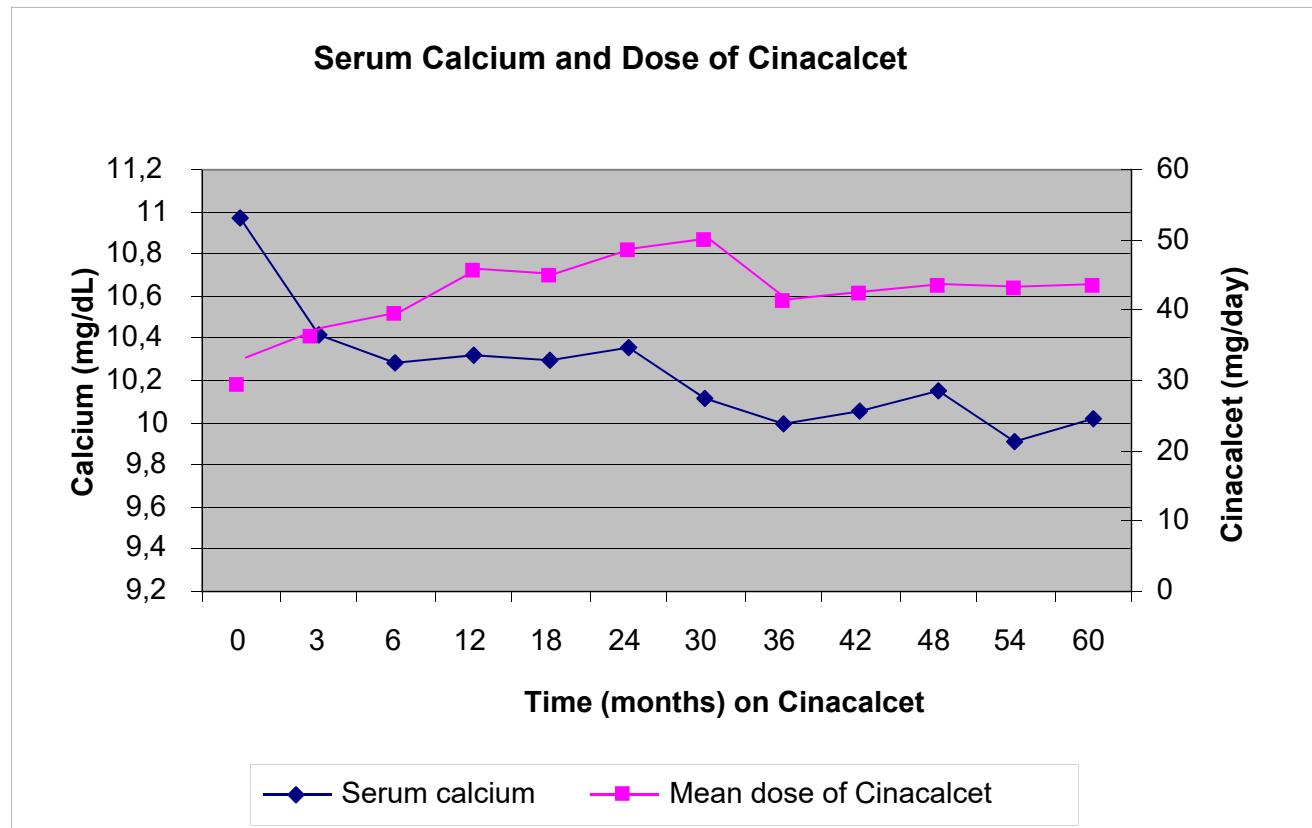
## Cinacalcet controla hiperCa

Randomized, double-blind, placebo-controlled, multicenter, phase III study



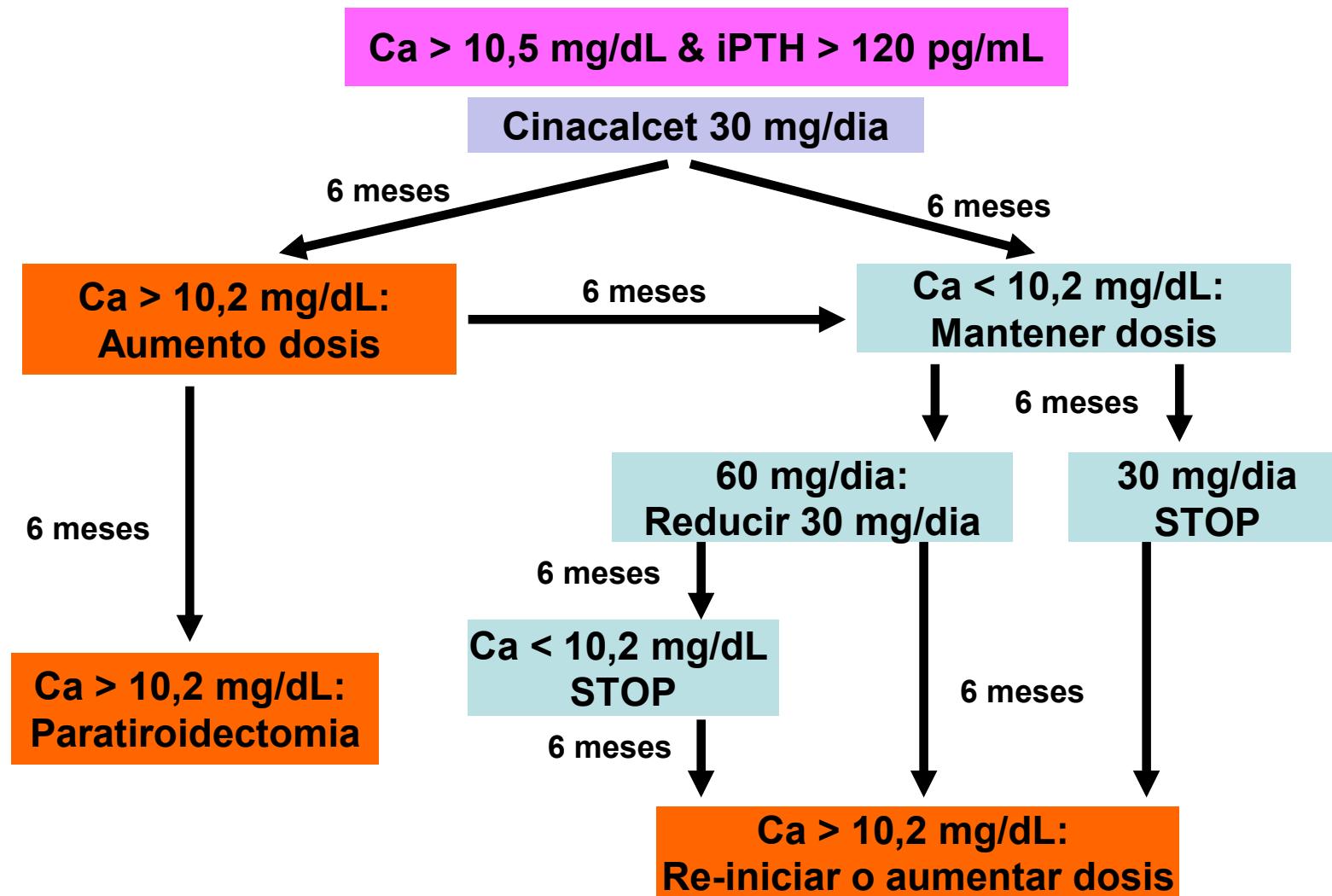
## Cinacalcet controla hiperCa a largo plazo

### Long-term follow-up





# Algoritmo manejo hiperCa postTR

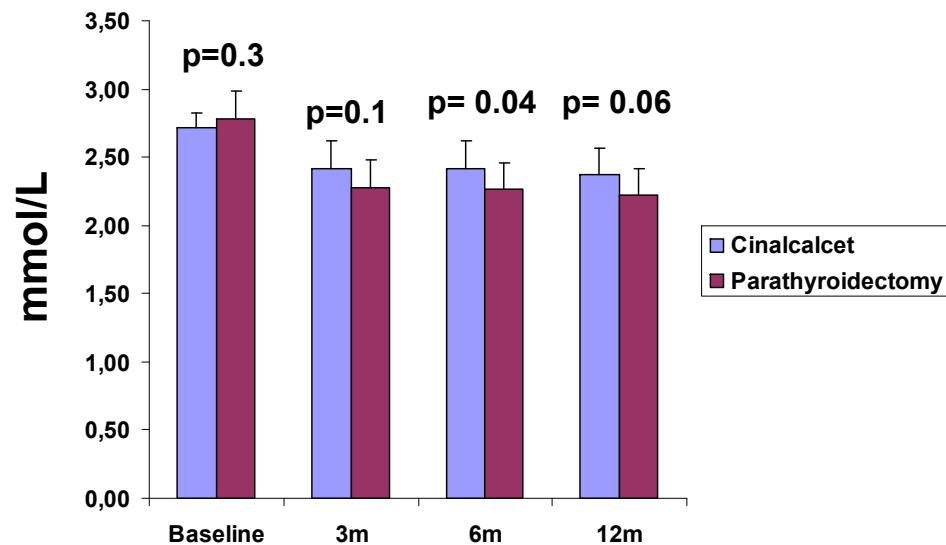


## Posibilidades de manejo de la hiperCa post TR

- Conducta expectante
- Calcimiméticos (Cinacalcet)
- Paratiroidectomia

Randomized Study Comparing Parathyroidectomy Versus Cinacalcet

Mayor descenso Ca con PTx

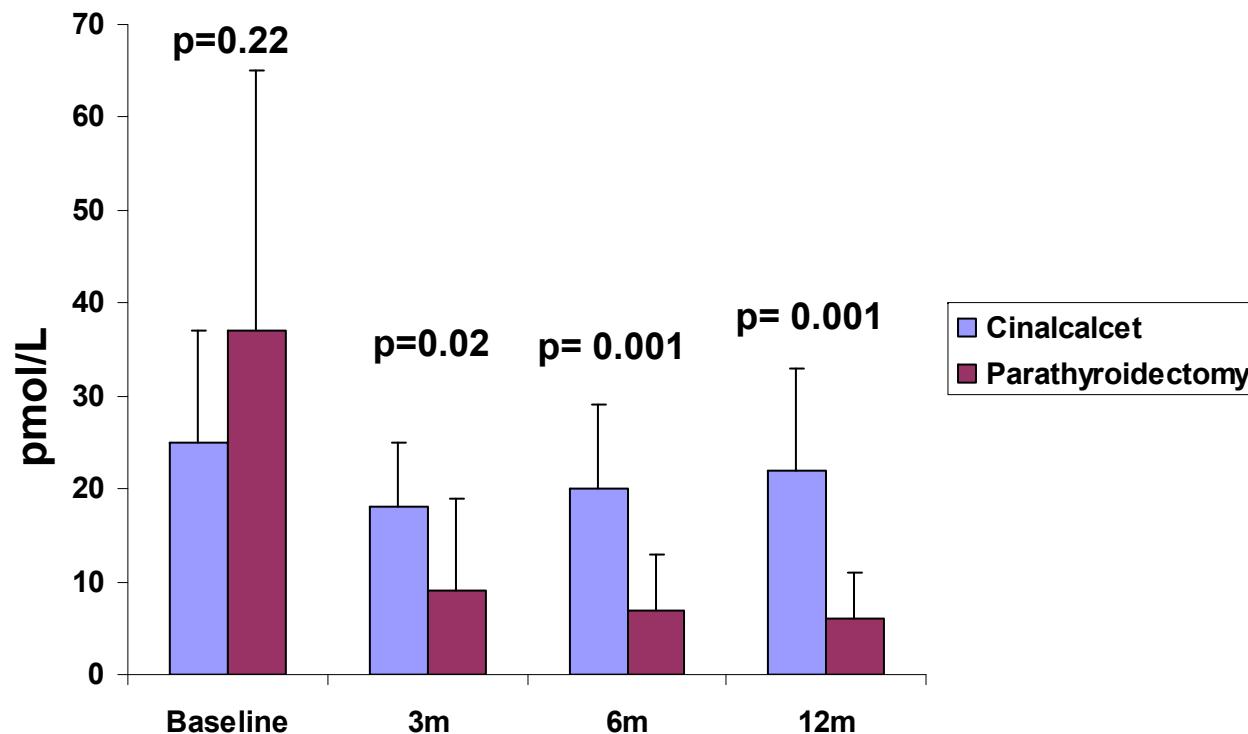


Normocalcemia (12 months): 67% Cinacalcet and 100% Parathyroidectomy (p=0.04)

In parathyroidectomy group : - Hypocalcemia (n=40%) (10% requiring hospitalization )  
-Transient dysphonia (n=2)

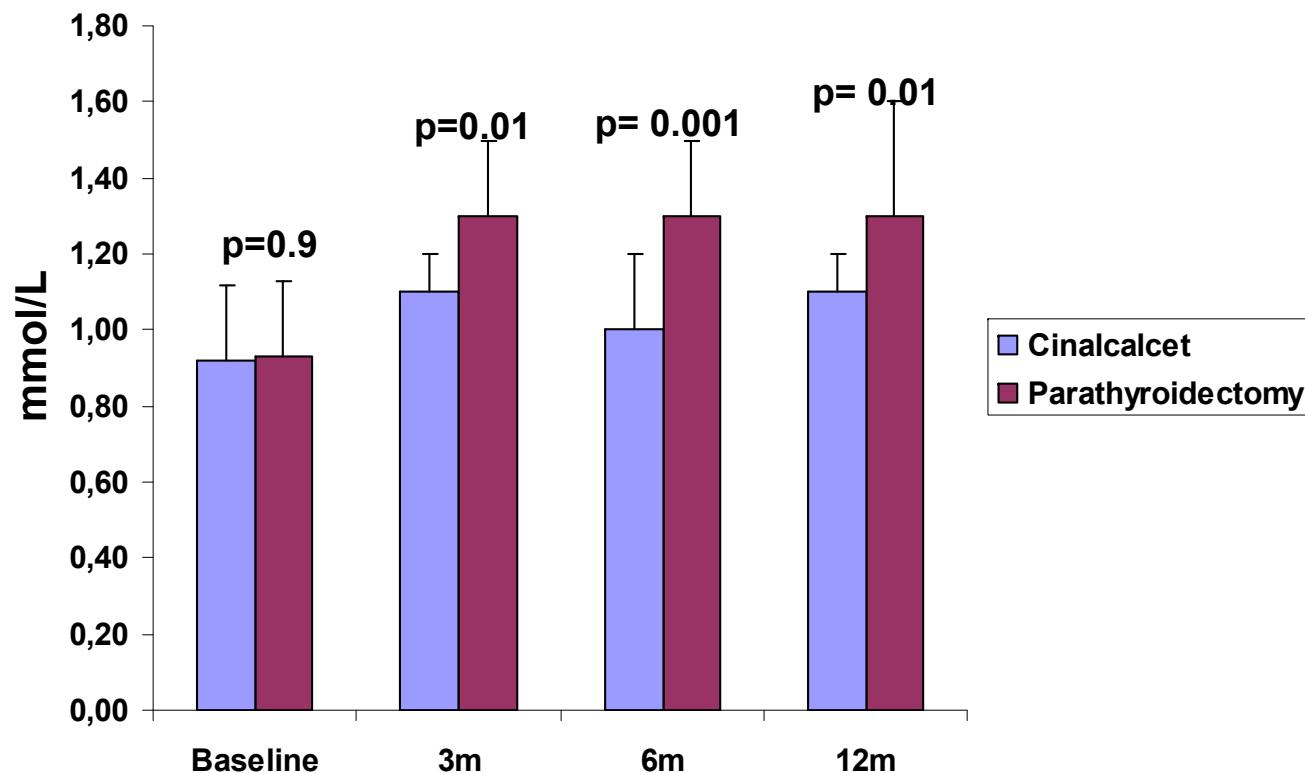
Randomized Study Comparing Parathyroidectomy Versus Cinacalcet

Mayor descenso de PTH con PTx

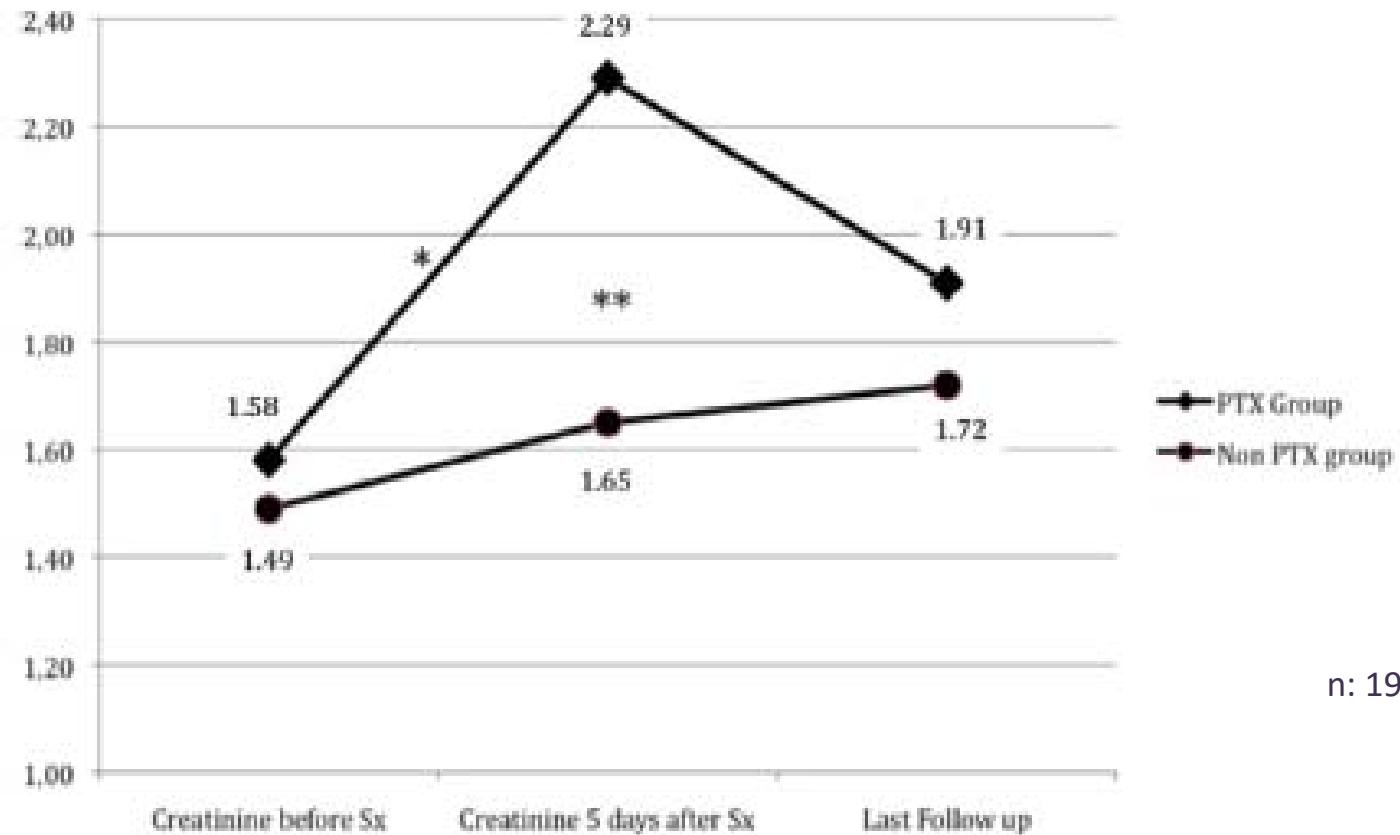


Randomized Study Comparing Parathyroidectomy Versus Cinacalcet

Mayor incremento de P con PTx



## Aumento de creatinina trás paratiroidectomia



## Manejo hiperCa post TR

|   | Observation (n=52) | Cinacalcet (n=13) | PTX (n=18) | Total (n=83) | P                  |
|---|--------------------|-------------------|------------|--------------|--------------------|
| Pretreatment hypercalcemic complications, n (%) |                    |                   |            |              | <0.01 <sup>a</sup> |
| Abdominal pain                                  | 8 (15.38)          | 3 (23.08)         | 7 (38.89)  | 18 (21.69)   |                    |
| Osteopenia/osteoporosis                         | 7 (13.46)          | 4 (30.77)         | 5 (27.78)  | 16 (19.28)   |                    |
| Fatigue   | 4 (7.69)           | 6 (46.15)         | 1 (5.56)   | 11 (13.25)   |                    |
| Admission for IVF                               | 4 (7.69)           | 1 (7.69)          | 6 (33.33)  | 11 (13.25)   |                    |
| Depression                                      | 2 (3.85)           | 3 (23.08)         | 2 (11.11)  | 7 (8.43)     |                    |
| Fracture  | 1 (1.92)           | 2 (15.38)         | 3 (16.67)  | 6 (7.23)     |                    |
| Kidney stones                                   | 3 (5.77)           | 0 (0.00)          | 2 (11.11)  | 5 (6.02)     |                    |
| Change in MS                                    | 0 (0.00)           | 2 (15.38)         | 1 (5.56)   | 3 (3.61)     |                    |
| EKG changes                                     | 0 (0.00)           | 0 (0.00)          | 1 (5.56)   | 1 (1.20)     |                    |
| Posttreatment complications, n (%)              |                    |                   |            |              | <0.01 <sup>a</sup> |
| Continued symptoms                              | 13 (25.00)         | 1 (7.69)          | 0 (0.00)   | 14 (16.87)   |                    |
| Acute kidney failure                            | 2 (3.85)           | 0 (0.00)          | 1 (5.56)   | 3 (3.61)     |                    |
| Graft failure                                   | 7 (13.46)          | 1 (7.69)          | 0 (0.00)   | 8 (9.64)     |                    |
| Death   | 4 (7.69)           | 0 (0.0)           | 1 (5.56)   | 5 (6.02)     |                    |
| Reoperation for recurrent disease               | 0 (0.0)            | 0 (0.0)           | 2 (11.11)  | 2 (2.41)     |                    |
| Wound infection                                 | 0 (0.0)            | 0 (0.0)           | 1 (5.56)   | 1 (1.20)     |                    |
| Paresthesia                                     | 0 (0.0)            | 0 (0.0)           | 3 (16.67)  | 3 (3.61)     |                    |
| Calcium supplements                             | 0 (0.0)            | 0 (0.0)           | 4 (22.22)  | 4 (4.82)     |                    |
| Hungry bone syndrome                            | 0 (0.0)            | 0 (0.0)           | 1 (5.56)   | 1 (1.20)     |                    |
| Transient voice hoarseness                      | 0 (0.0)            | 0 (0.0)           | 1 (5.56)   | 1 (1.20)     |                    |

<sup>a</sup> Significance based on Fisher exact test.

EKG, electrocardiographic; IVF, intravenous fluid; MS, mental status; PTX, parathyroidectomy.

## Manejo hiperCa post TR

| <b>Paratiroidectomia</b>    |  | <b>Cinacalcet</b>  |  |
|-----------------------------|--|--|--|
| <b>Ventaja</b>              | <b>Inconveniente</b>   | <b>Ventaja</b>   | <b>Inconveniente</b>                                   |
| <b>Buen control hiperCa</b> | <b>-Puede disminuir FG<br/>-Riesgo hipoCa<br/>-Riesgo quirurg<br/><br/>-Recidiva</b> | <b>Control Ca Seguro<br/><br/>Reducción tamaño gland.?</b> | <b>Tolerancia<br/><br/>Necesidad trat. persistente</b> |

## **Alteraciones óseo-metabólicas más frecuentes post TR:**

- **Hipercalcemia**
- **Hipofosfatemia**
- **Pérdida de masa ósea. Fracturas**

## Fosfatemia post TR

### Evolución del balance mineral en los 3 m postrasplante

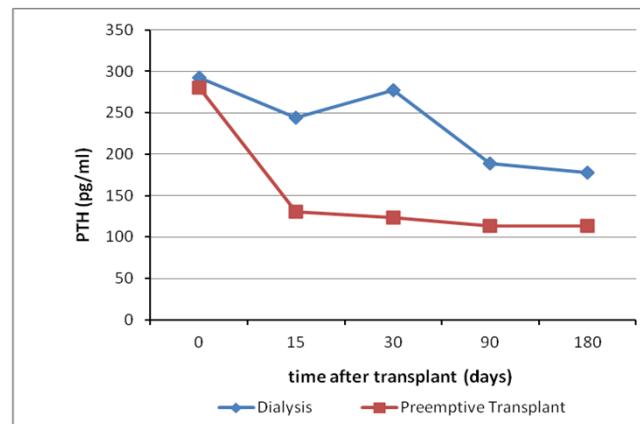
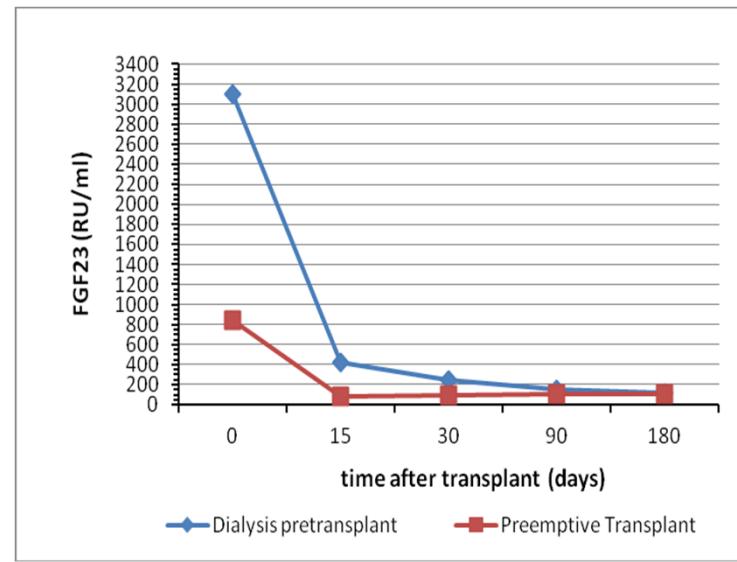
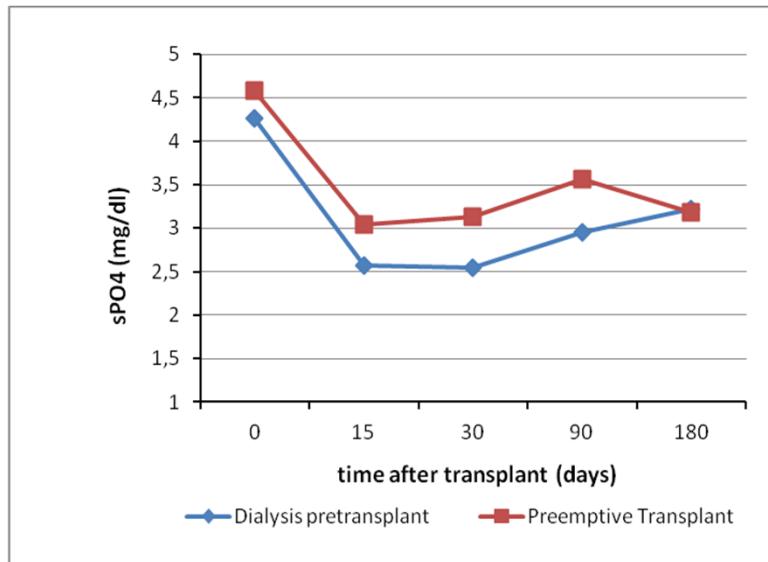
Table 3. Parameters of mineral metabolism at the time of transplantation and at 3 mo<sup>a</sup>

| Parameter   | Transplantation | 3 Mo          | P       |
|---|-----------------|---------------|---------|
| PO <sub>4</sub> (mg/dl)                           | 4.8 ± 1.2       | 2.7 ± 0.7     | <0.0001 |
| Albumin (g/dl)                                    | 44.1 ± 5.3      | 43.1 ± 3.7    | 0.0100  |
| Ca (mg/dl)  | 9.59 ± 0.70     | 9.69 ± 0.59   | 0.0100  |
| Ca below/on/above K/DOQI targets (%)              | 9.0/41.8/49.3   | 1.0/85.6/13.4 | <0.0001 |
| Ca <sub>c</sub> (mg/dl)                           | 9.29 ± 0.80     | 9.44 ± 0.57   | <0.0001 |
| Ca <sub>c</sub> below/on/above K/DOQI targets (%) | 11.4/53.2/35.3  | 7.0/86.1/7.0  | <0.0001 |
| hypercalcemia (>10.3 mg/dl; %)                    | 9.0             | 7.0           | 0.4600  |

n: 201

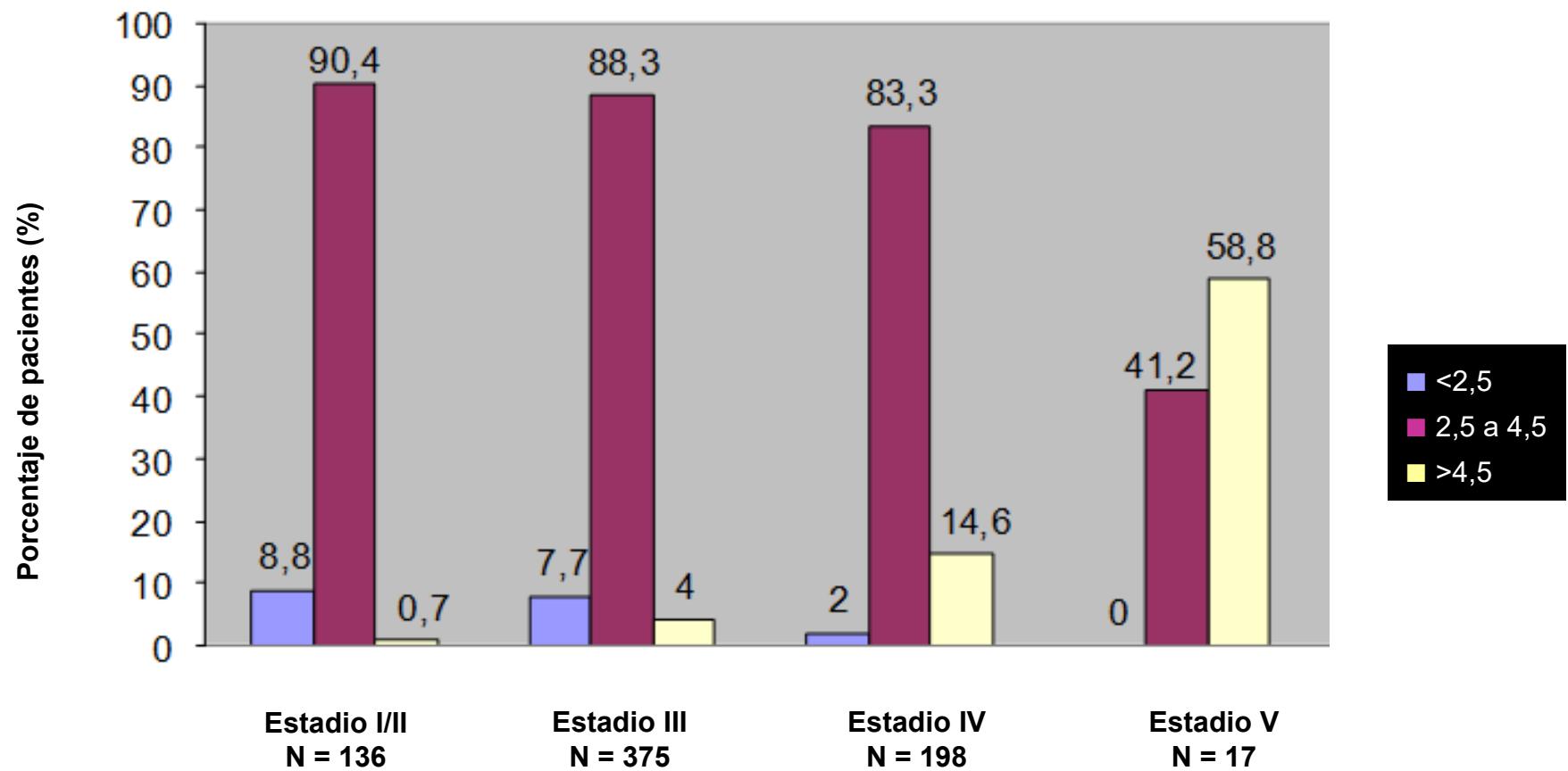
## Fosfatemia post TR

FGF23 preTR condiciona mayor hipoP postTR precoz  
PTH la condiciona a más largo plazo



## Fosfatemia post TR

HipoP se relaciona con función renal  
(a mejor función renal más % hipoP)

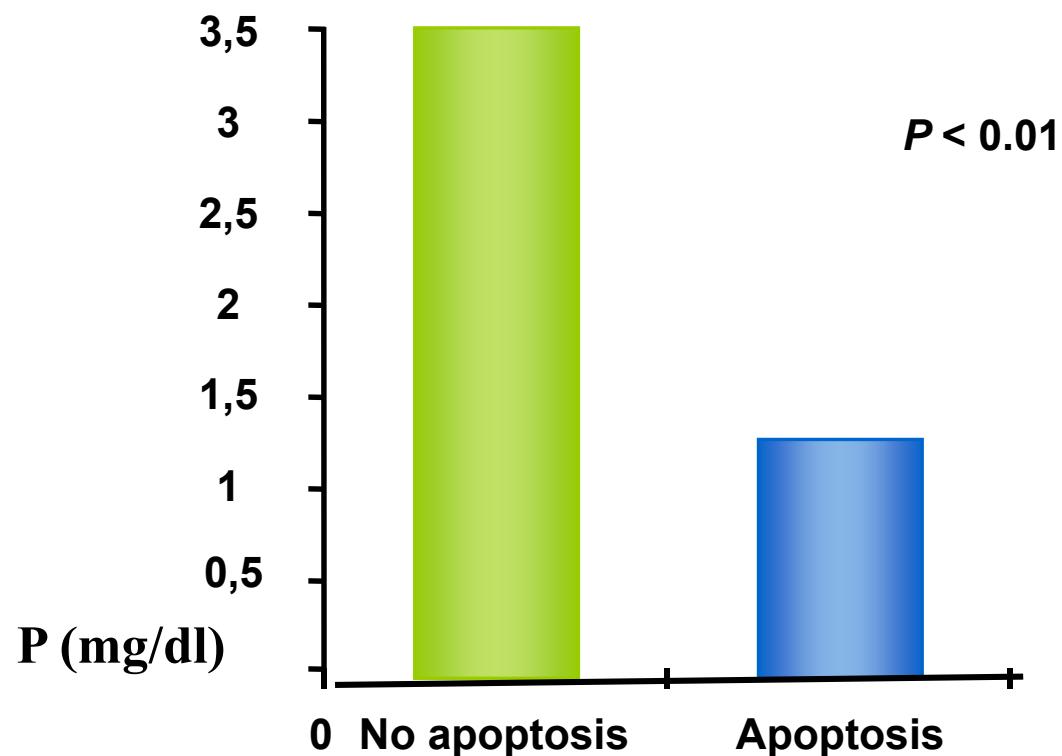


Torres A, Torregrosa JV, et al. Nefrologia 2016;36:255-67.

JV Torregrosa. Hospital Clinic. Barcelona

## Fosfatemia post TR

Fósforo post TR y apoptosis osteoblastos

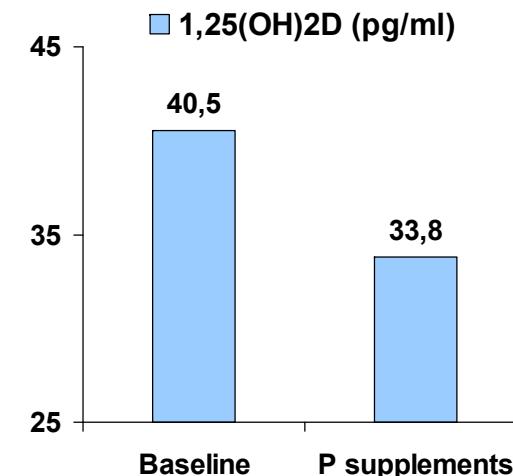
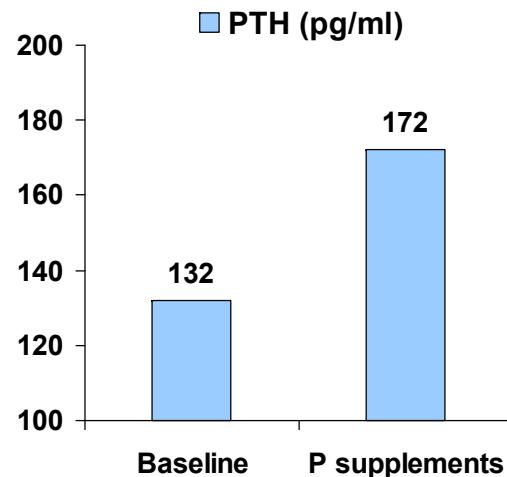
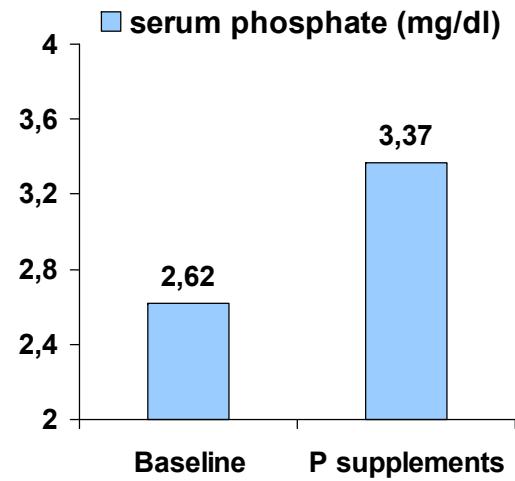


Rojas E, et al Kidney Int 2003;63:1915-23.

JV Torregrosa. Hospital Clinic. Barcelona

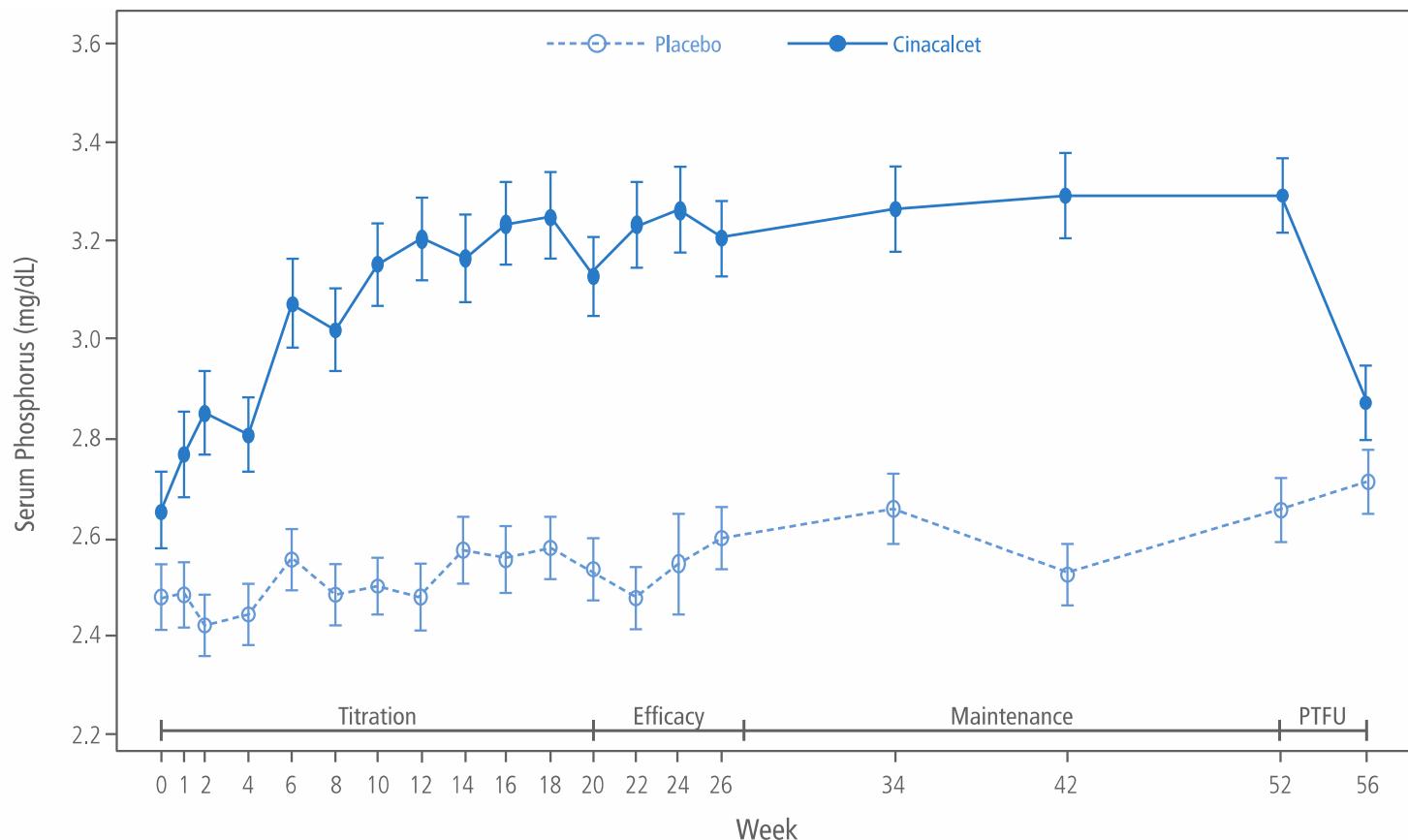
## Fosfatemia post TR

La administración oral de P no es lo más aconsejable



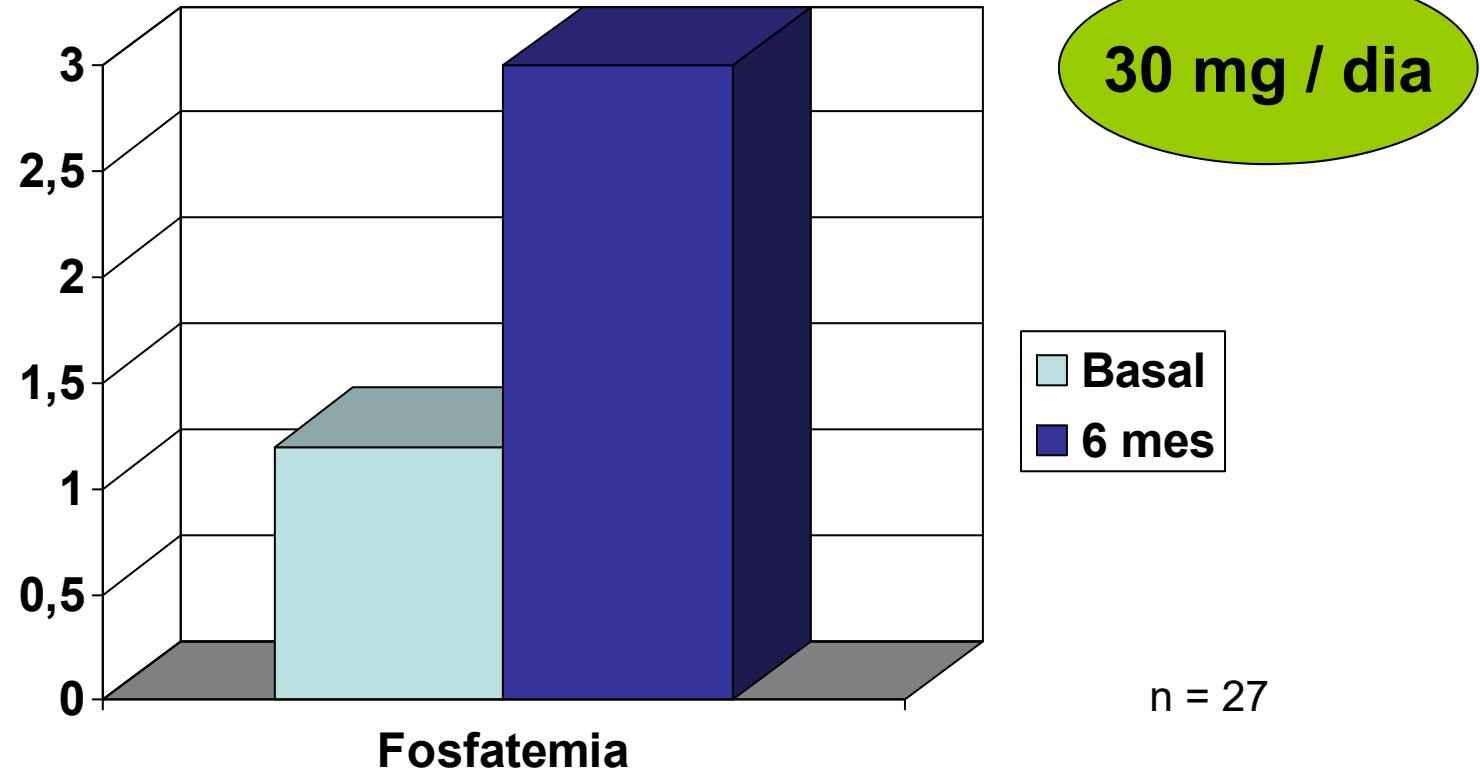
## Fosfatemia post TR

### Cinacalcet mejora hipoP



**Randomized, double-blind, placebo-controlled, multicenter, phase III study**

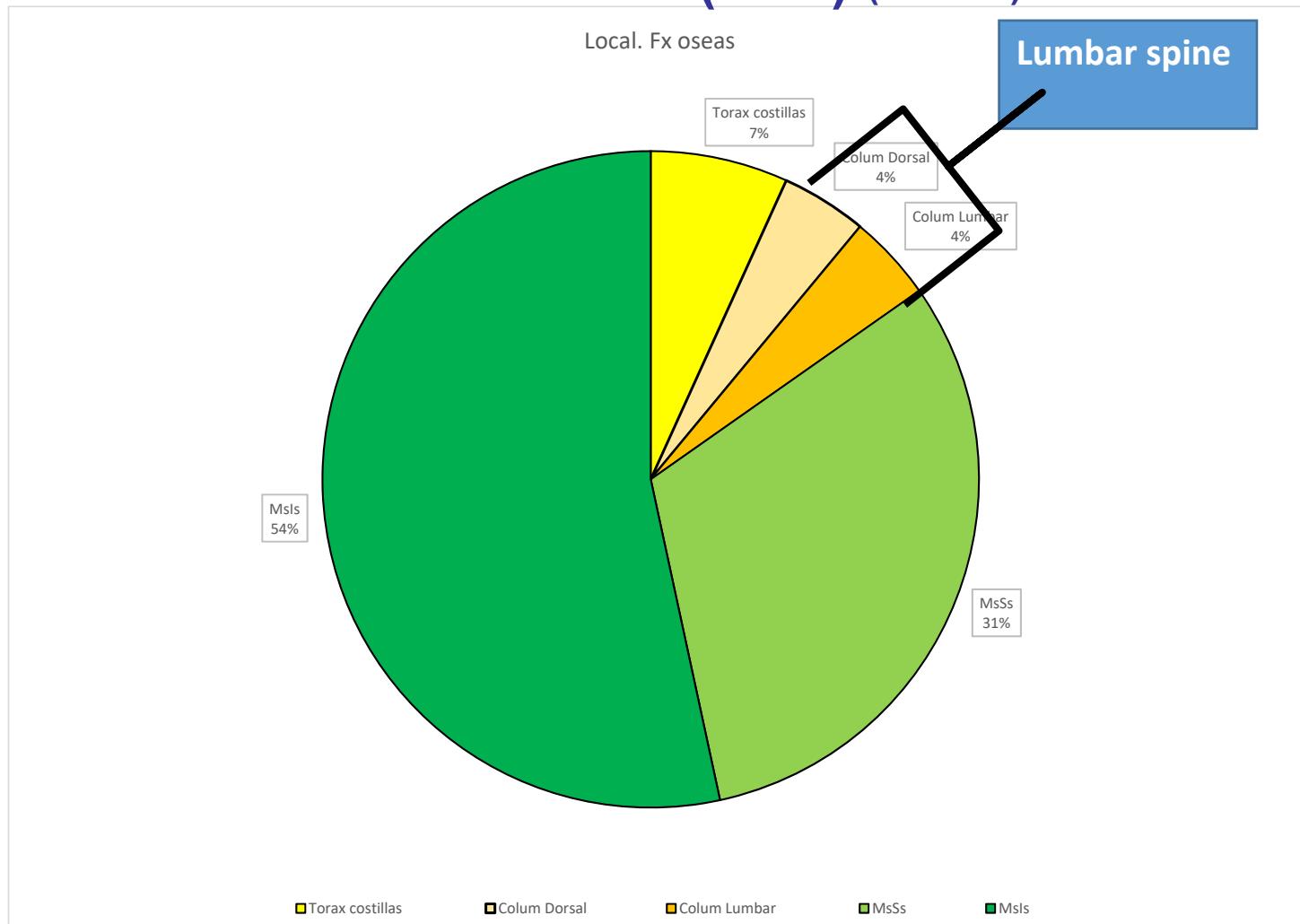
## Cinacalcet mejora hipoP



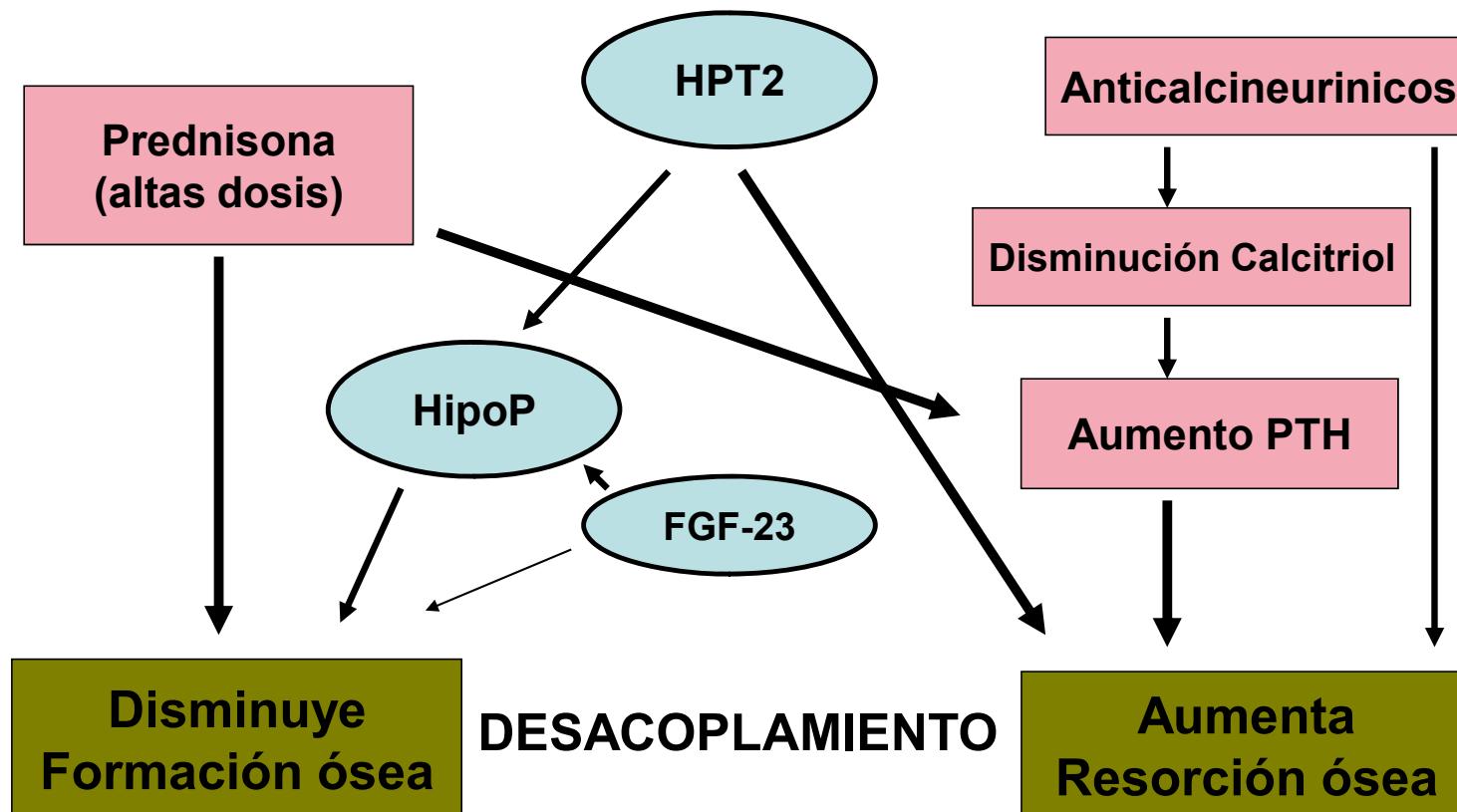
## **Alteraciones óseo-metabólicas más frecuentes post TR:**

- **Hipercalcemia**
- **Hipofosfatemia**
- **Pérdida de masa ósea. Fracturas**

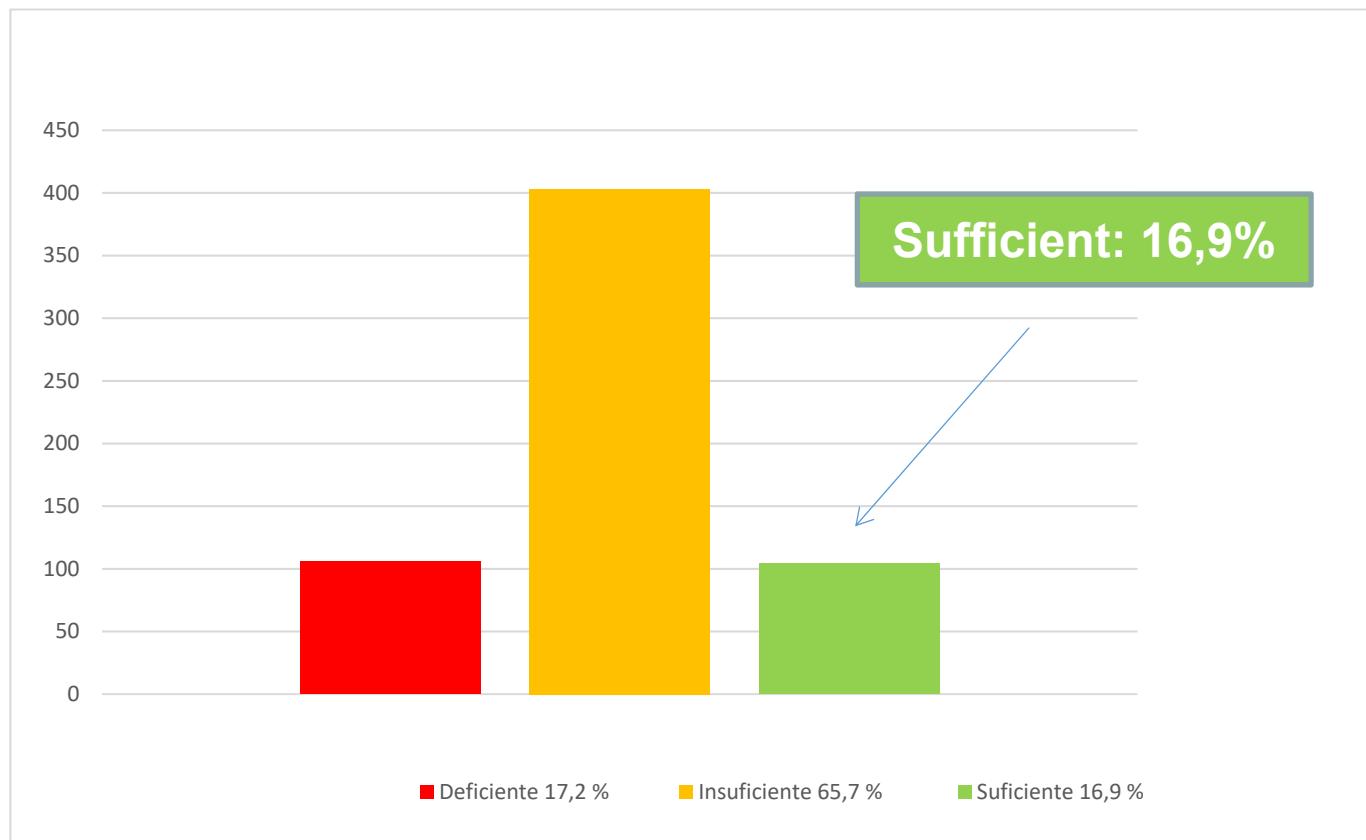
## Fracturas (12%) (n=1001)



## Fisiopatología de la disminución de la masa ósea posTR



## Correlación positiva de vit. D y fracturas

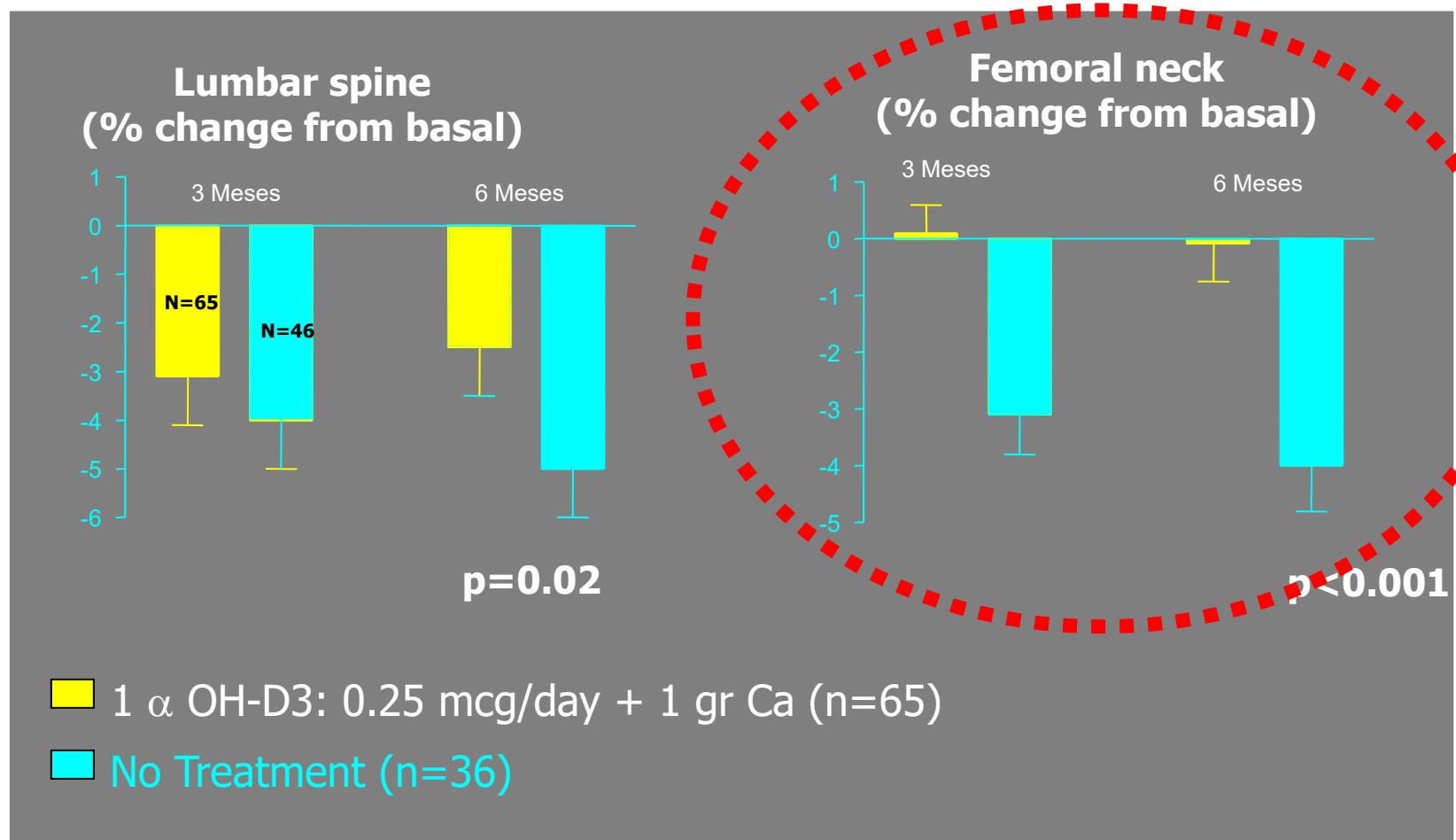


## Alternativas de tratamiento

**Vitamina D + Ca**  
**Fármacos antiresortivos**  
- **Bifosfonatos**  
- **Denosumab**

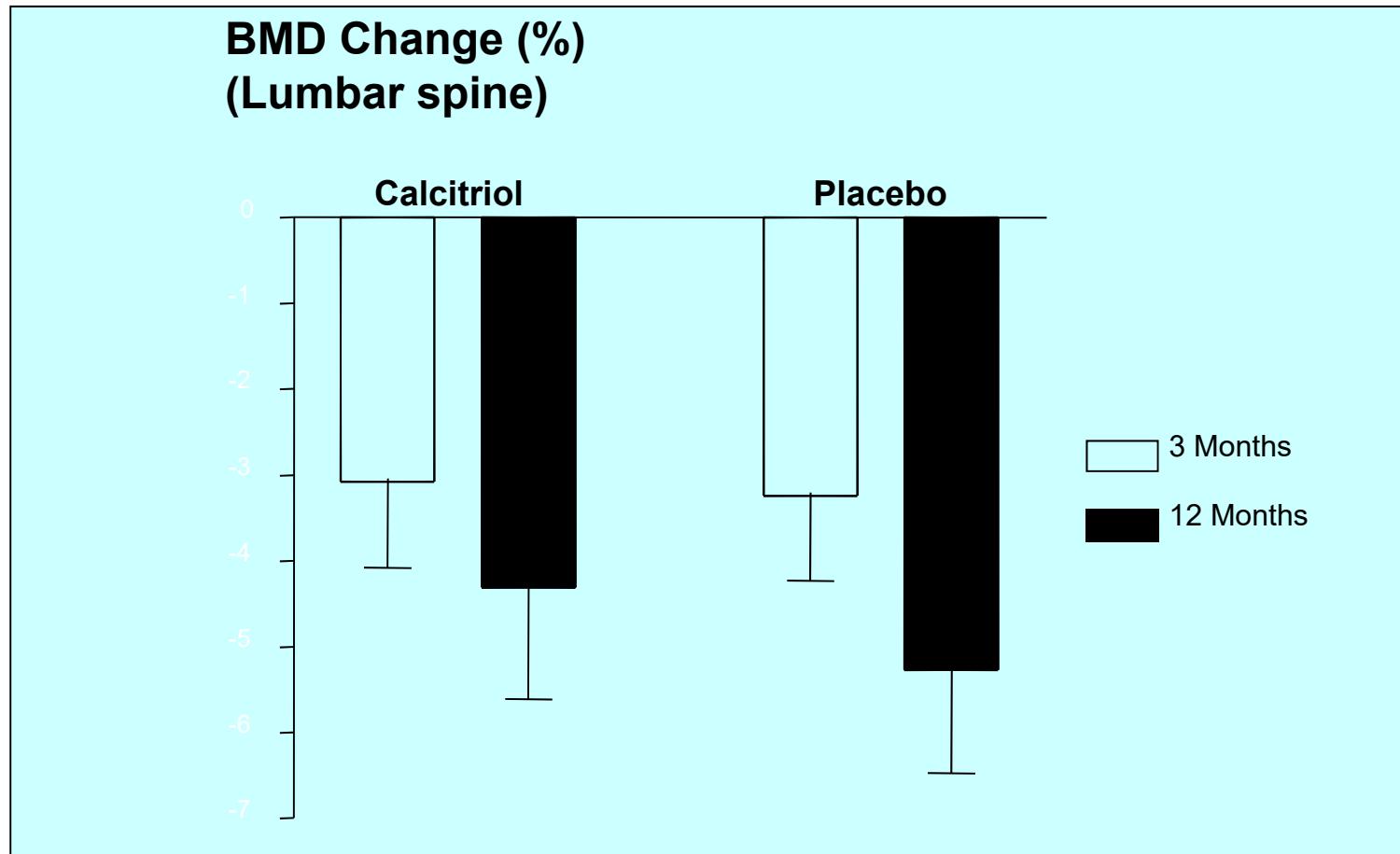
## Vitamina D + Ca

### BMD (Alfacalcidol / Placebo)



## Vitamina D + Ca

### BMD Lumbar spine (Calcitriol / Placebo)

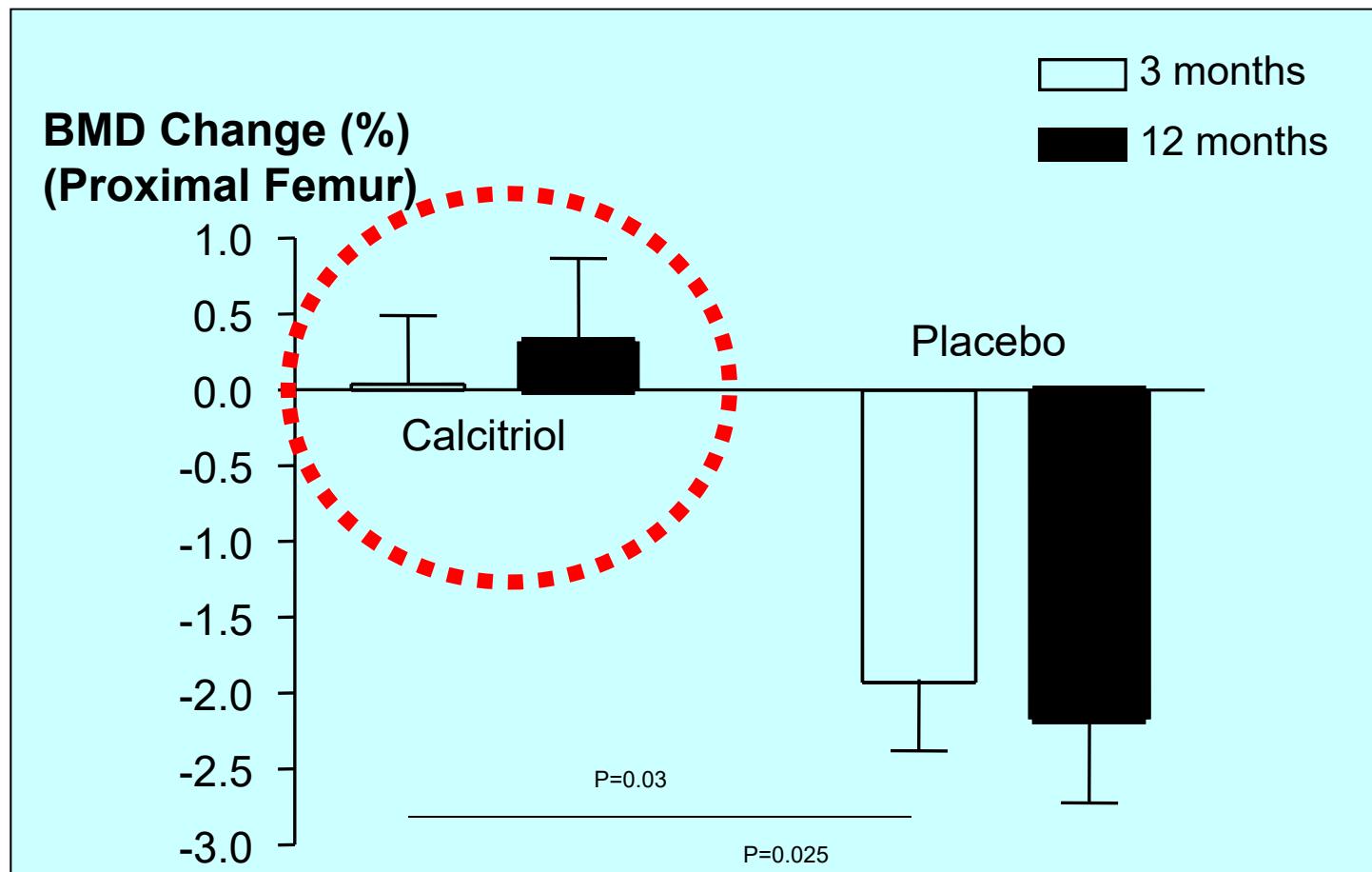


Torres A, et al. Kidney Int 2004;65:705

JV Torregrosa. Hospital Clinic. Barcelona

## Vitamina D + Ca

### BMD Femoral neck (Calcitriol / Placebo)



Torres A, et al. Kidney Int 2004;65:705

JV Torregrosa. Hospital Clinic. Barcelona

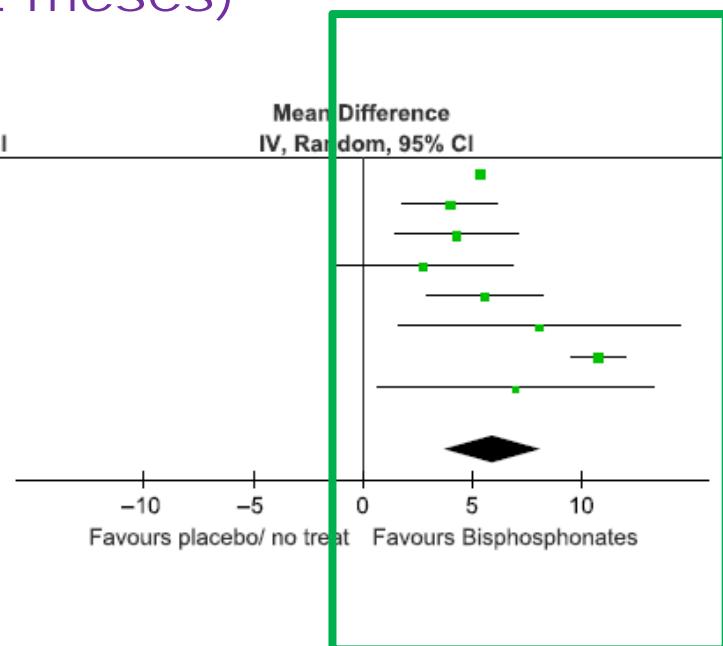
# Bifosfonatos en TR

## Densidad mineral ósea (Columna lumbar -12 meses)

| Study or Subgroup     | Bisphosphonates |      |       | Placebo or No treatment |      |               | Mean Difference<br>IV, Random, 95% CI | Mean Difference<br>IV, Random, 95% CI |
|-----------------------|-----------------|------|-------|-------------------------|------|---------------|---------------------------------------|---------------------------------------|
|                       | Mean            | SD   | Total | Mean                    | SD   | Total         |                                       |                                       |
| Coco 2003             | -0.39           | 0.05 | 31    | -5.81                   | 0.09 | 28            | 17.1%<br>5.42 [5.38, 5.46]            |                                       |
| El-Agroudy 2005       | 0.8             | 3.05 | 15    | -3.2                    | 3.05 | 15            | 14.7%<br>4.00 [1.82, 6.18]            |                                       |
| Giannini 2001         | 5               | 4.4  | 20    | 0.7                     | 4.4  | 18            | 13.4%<br>4.30 [1.50, 7.10]            |                                       |
| Grotz 1998            | 4.6             | 5.3  | 15    | 1.8                     | 5.9  | 14            | 10.8%<br>2.80 [-1.29, 6.89]           |                                       |
| Grotz 2001            | -0.9            | 6.1  | 36    | -6.5                    | 5.4  | 36            | 13.7%<br>5.60 [2.94, 8.26]            |                                       |
| Koc 2002              | 8.15            | 9.2  | 8     | 0.06                    | 1.41 | 8             | 7.0%<br>8.09 [1.64, 14.54]            |                                       |
| Nam 2000              | 2.6             | 1.4  | 15    | -8.2                    | 2.3  | 20            | 16.3%<br>10.80 [9.57, 12.03]          |                                       |
| Torregrosa 2011       | 1               | 8.3  | 19    | -6                      | 8.3  | 10            | 7.1%<br>7.00 [0.64, 13.36]            |                                       |
| <b>Total (95% CI)</b> | <b>159</b>      |      |       | <b>149</b>              |      | <b>100.0%</b> | <b>5.98 [3.77, 8.18]</b>              |                                       |

Heterogeneity:  $\tau^2 = 7.42$ ;  $\chi^2 = 77.92$ , df = 7 ( $P < 0.00001$ );  $I^2 = 91\%$

Test for overall effect:  $Z = 5.30$  ( $P < 0.00001$ )



## Mejoría de la DMO

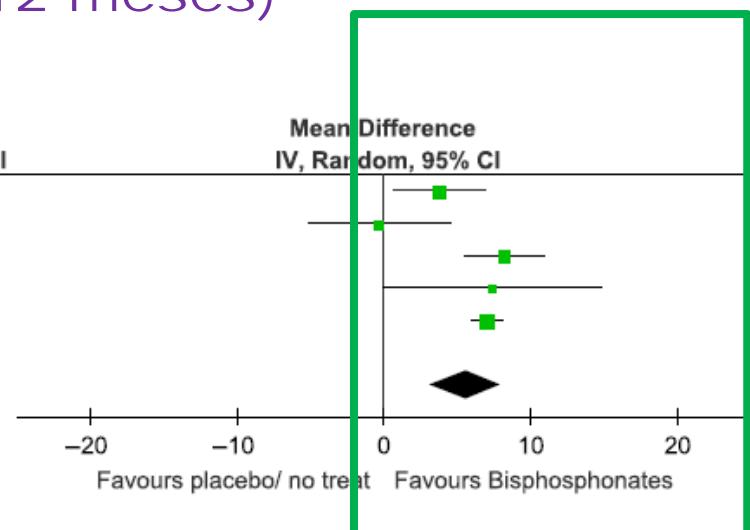
## Bifosfonatos en TR

### Densidad mineral ósea (Cuello femoral -12 meses)

| Study or Subgroup     | Experimental |       |       | Control   |      |               | Mean Difference<br>IV, Random, 95% CI |
|-----------------------|--------------|-------|-------|-----------|------|---------------|---------------------------------------|
|                       | Mean         | SD    | Total | Mean      | SD   | Total         |                                       |
| Giannini 2001         | 4.5          | 4.9   | 20    | 0.7       | 4.9  | 18            | 21.8%<br>3.80 [0.68, 6.92]            |
| Grotz 1998            | -1.1         | 5.5   | 15    | -0.8      | 7.6  | 14            | 14.5%<br>-0.30 [-5.16, 4.56]          |
| Grotz 2001            | 0.5          | 5.2   | 36    | -7.7      | 6.5  | 36            | 23.8%<br>8.20 [5.48, 10.92]           |
| Koc 2002              | 9.34         | 10.47 | 8     | 1.95      | 2.52 | 8             | 8.1%<br>7.39 [-0.07, 14.85]           |
| Nam 2000              | 1.9          | 0.8   | 15    | -5.1      | 2.2  | 20            | 31.8%<br>7.00 [5.95, 8.05]            |
| <b>Total (95% CI)</b> | <b>94</b>    |       |       | <b>96</b> |      | <b>100.0%</b> | <b>5.57 [3.12, 8.01]</b>              |

Heterogeneity:  $\tau^2 = 4.59$ ;  $\chi^2 = 12.78$ , df = 4 ( $P = 0.01$ );  $I^2 = 69\%$

Test for overall effect:  $Z = 4.47$  ( $P < 0.00001$ )

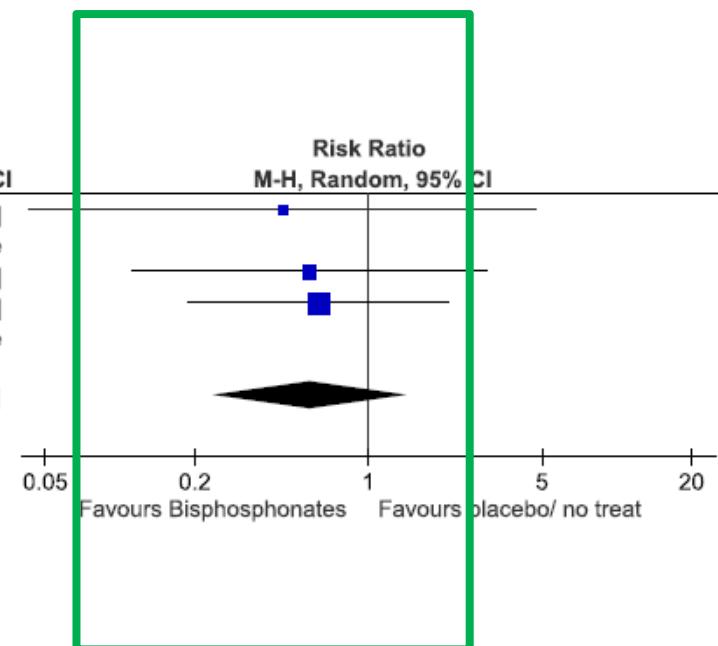


Mejoría de la DMO

# Bifosfonatos en TR

## Fracturas vertebrales (12 meses)

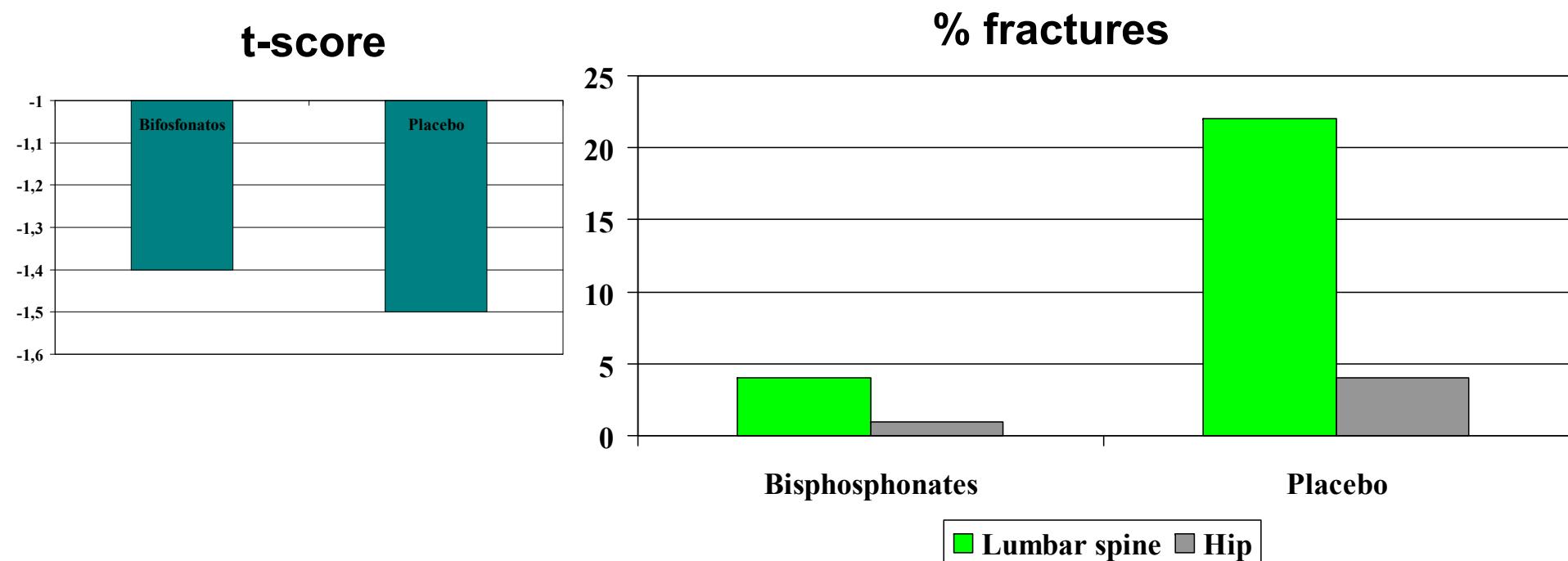
| Study or Subgroup        | Bisphosphonates  |            | Placebo or No treatment |            | Weight        | Risk Ratio<br>M-H, Random, 95% CI |
|--------------------------|--|------------|-------------------------|------------|---------------|-----------------------------------|
|                          | Events   | Total      | Events                  | Total      |               |                                   |
| Coco 2003                | 1  | 31         | 2                       | 28         | 14.6%         | 0.45 [0.04, 4.71]                 |
| Shahidi 2015             | 0  | 16         | 0                       | 24         |               | Not estimable                     |
| Torregrosa 2007          | 2  | 39         | 4                       | 45         | 29.8%         | 0.58 [0.11, 2.98]                 |
| Torregrosa 2010          | 4  | 52         | 6                       | 49         | 55.5%         | 0.63 [0.19, 2.09]                 |
| Torregrosa 2011          | 0  | 24         | 0                       | 15         |               | Not estimable                     |
| <b>Total (95% CI)</b>    | <b>7</b>   | <b>162</b> | <b>12</b>               | <b>161</b> | <b>100.0%</b> | <b>0.58 [0.24, 1.43]</b>          |
| Total events             | 7  |            | 12                      |            |               |                                   |
| Heterogeneity:           | $\tau^2 = 0.00$ ; $\chi^2 = 0.06$ , df = 2 ( $P = 0.97$ ); $I^2 = 0\%$ |            |                         |            |               |                                   |
| Test for overall effect: | $Z = 1.18$ ( $P = 0.24$ )  |            |                         |            |               |                                   |



Menor número de fracturas

## Bifosfonatos en TR

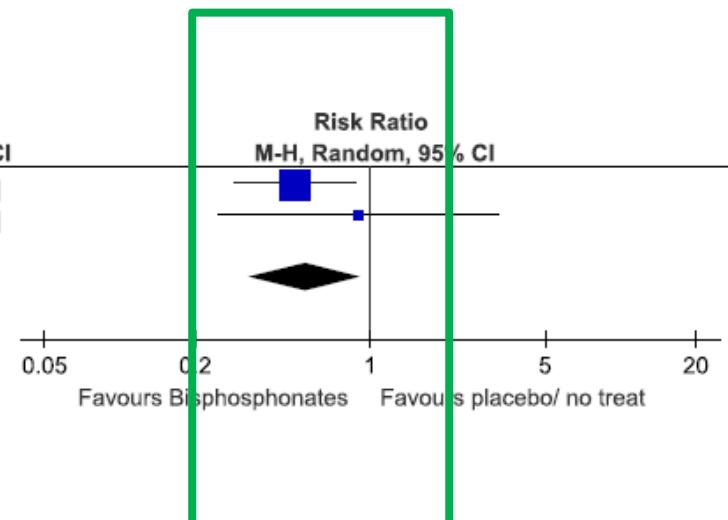
### Fracturas en pacientes de riesgo (% 5 años)



## Bifosfonatos en TR

### Episodios de rechazo agudo (confirmados por biopsia)

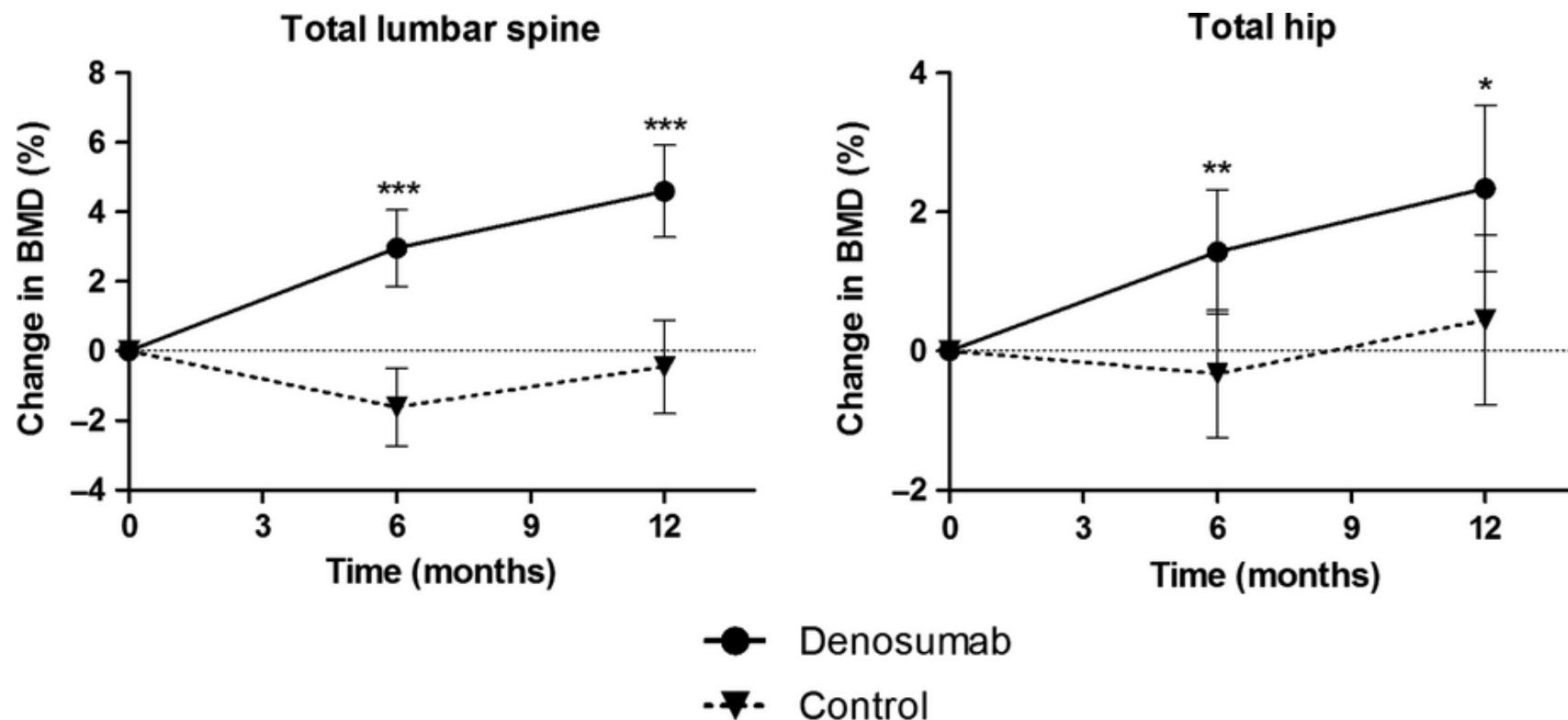
| Study or Subgroup        | Bisphosphonates  |           |        | Placebo or No treatment |               |                          | Risk Ratio<br>M-H, Random, 95% CI |
|--------------------------|--|-----------|--------|-------------------------|---------------|--------------------------|-----------------------------------|
|                          | Events   | Total     | Events | Total                   | Weight        |                          |                                   |
| Grotz 2001               | 11   | 36        | 22     | 36                      | 84.2%         | 0.50 [0.29, 0.87]        |                                   |
| Lee 2004                 | 4  | 30        | 4      | 27                      | 15.8%         | 0.90 [0.25, 3.25]        |                                   |
| <b>Total (95% CI)</b>    |  | <b>66</b> |        | <b>63</b>               | <b>100.0%</b> | <b>0.55 [0.33, 0.91]</b> |                                   |
| Total events             | 15   |           | 26     |                         |               |                          |                                   |
| Heterogeneity:           | Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.69, df = 1 (P = 0.41); I <sup>2</sup> = 0% |           |        |                         |               |                          |                                   |
| Test for overall effect: | Z = 2.30 (P = 0.02)  |           |        |                         |               |                          |                                   |



Menor número rechazos agudos

# Denosumab

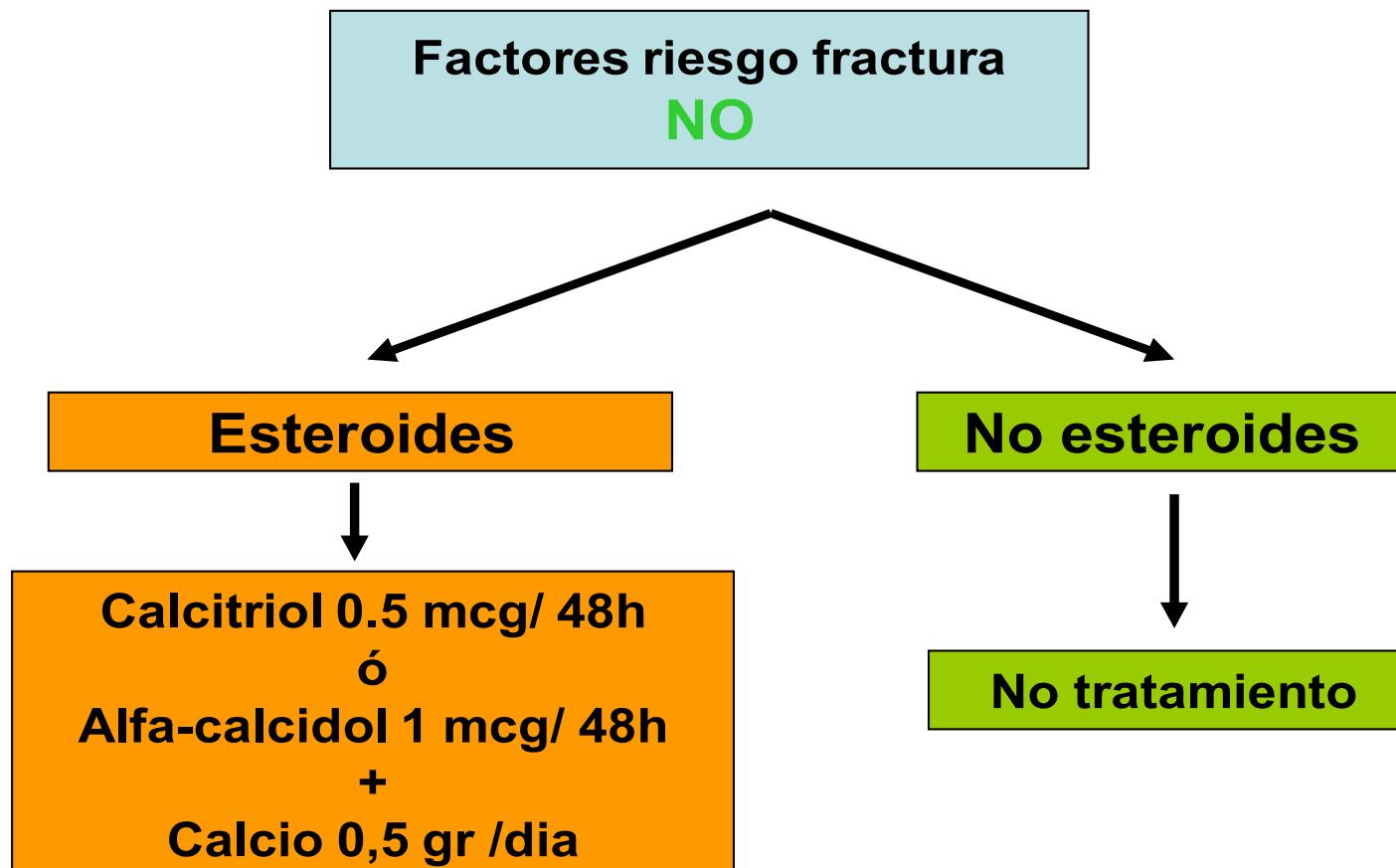
Densidad mineral ósea  
Franca mejoría en columna lumbar y cuello femoral



Effect of Twice-Yearly Denosumab on Prevention of Bone Mineral Density Loss in *De Novo* Kidney Transplant Recipients: A Randomized Controlled Trial



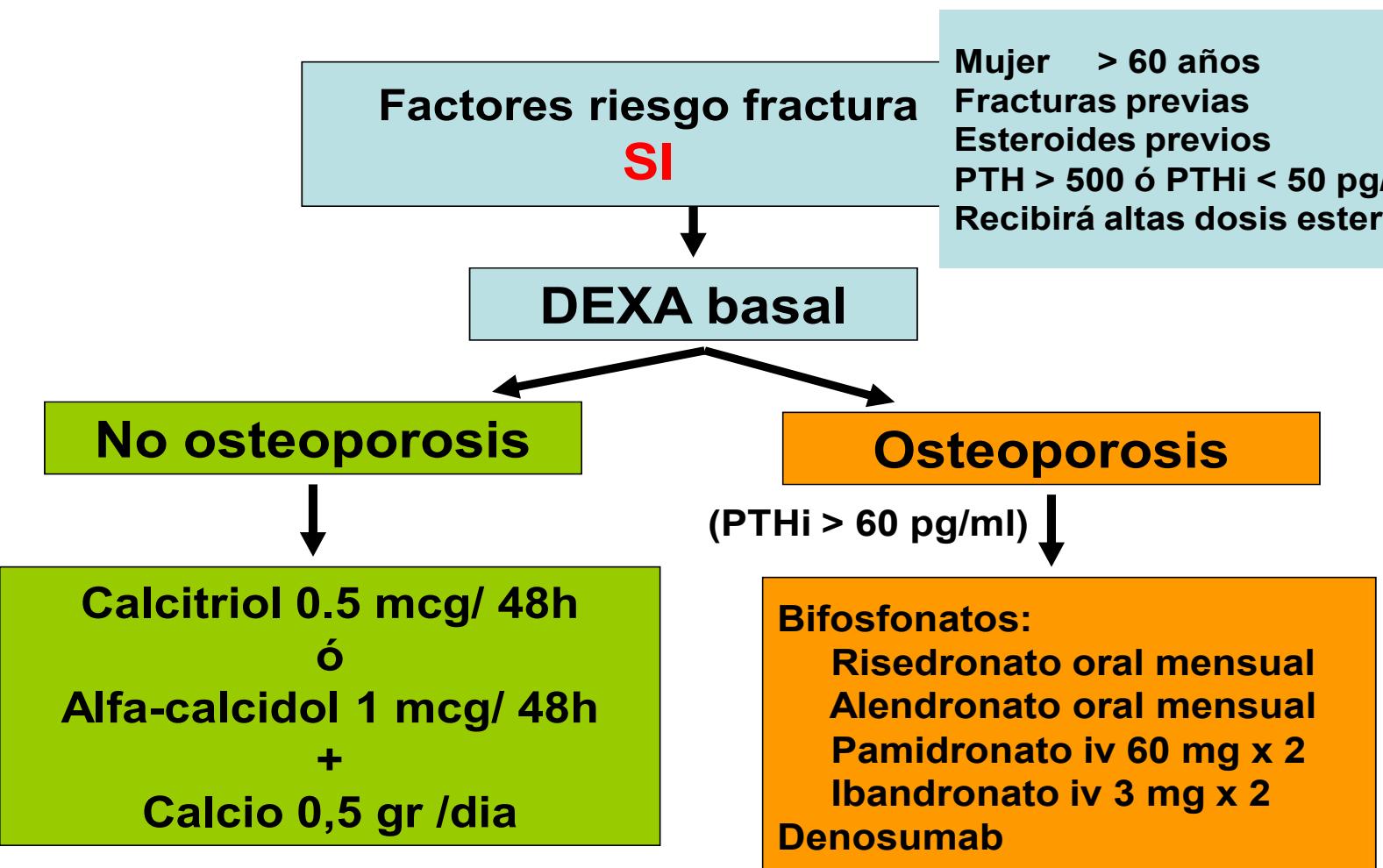
## Algoritmo de manejo de la prevención de pérdida de masa ósea postrasplante renal.



Adaptado de Torregrosa JV, et al. Nefrologia. 2011;31 Suppl 1:3-32

JV Torregrosa. Hospital Clinic. Barcelona

# Algoritmo de manejo de la prevención de pérdida de masa ósea postrasplante renal



Adaptado de Torregrosa JV, et al. Nefrologia. 2011;31 Suppl 1:3-32

JV Torregrosa. Hospital Clinic. Barcelona

## **Mensajes,**

### **Hipercalcemia:**

- ***Depende severidad HPT2º***
- ***Consecuencia negativas sobre hueso e in***
- ***Manejo:      Mantener valores adecuado  
Cinacalcet y si fracasa PTx***

### **Hipofosfatemia:**

- ***Depende de FGF-23 y PTH y de la funció***
- ***Manejo: evitar altas dosis P oral, Cinacal***

## **Mensajes,**

### **Pérdida masa ósea - Fracturas:**

- ***Prevalencia entre 10-15% (sobre todo fracturas)***
- ***Prevención***
  - ***Importante mantener valores adecuados de calcio y vitamina D***
  - ***Controlar PTH***
  - ***Evitar altas dosis de esteroides***
  - ***Emplear fármacos antiresortivos***

