Fármacos osteoformadores (el presente)

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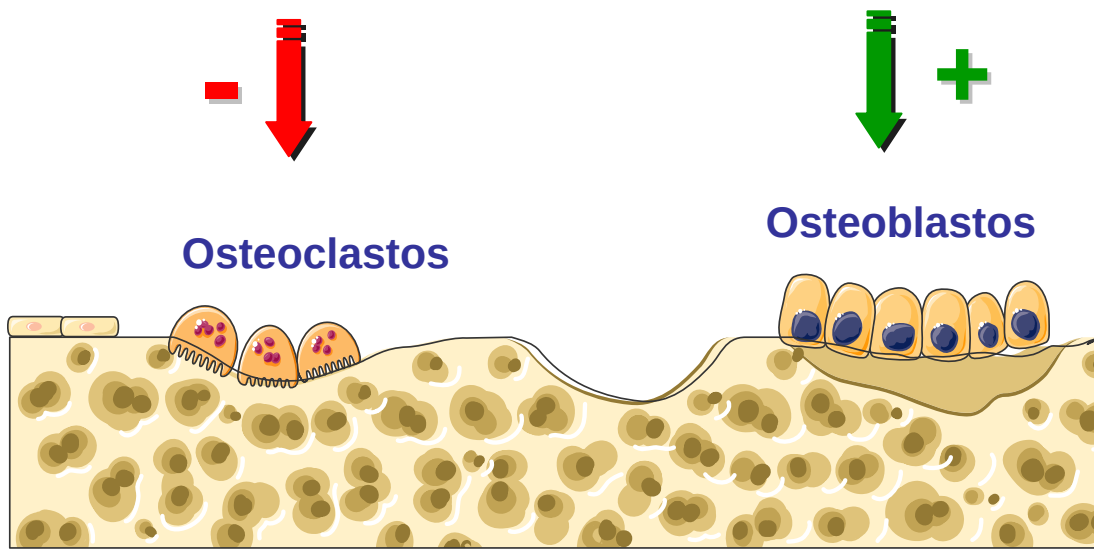
Tto. Osteoporosis (presente)

Anti-resortivos

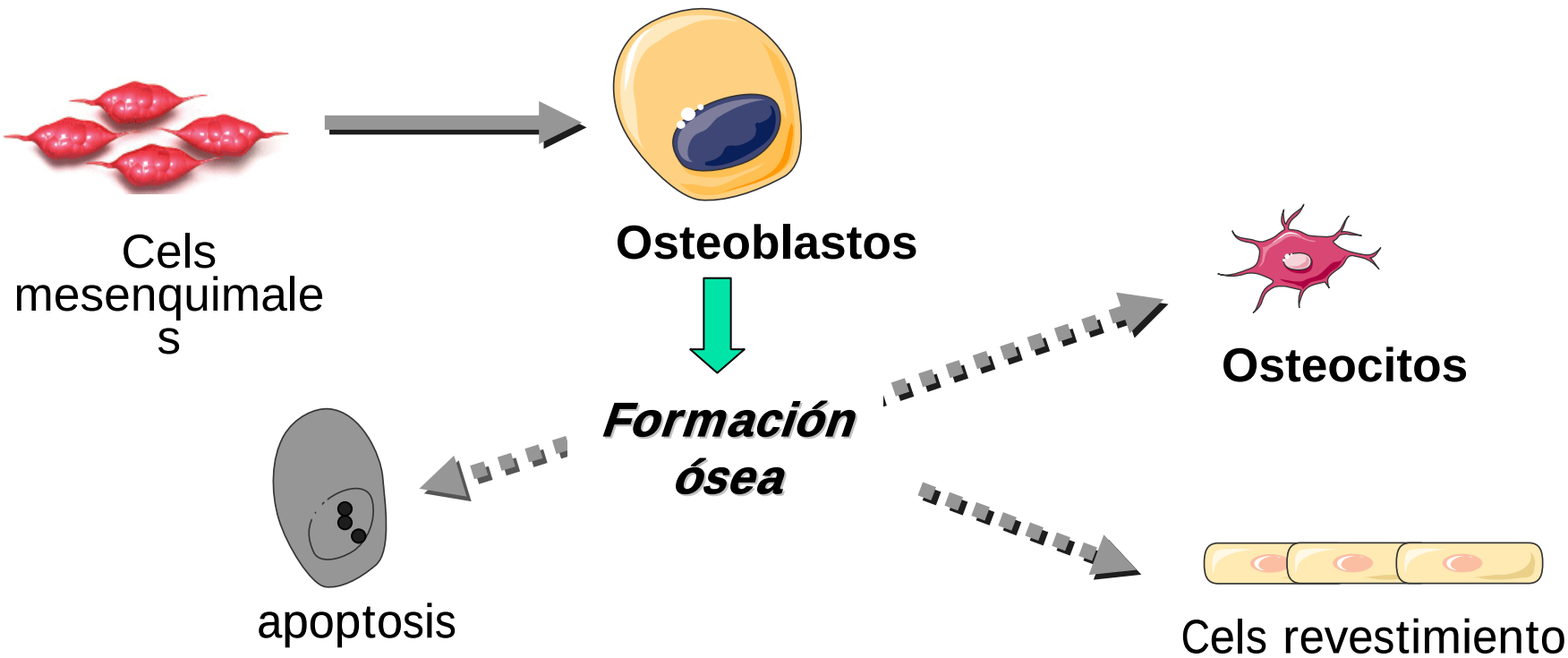
- (Calcio, vitamina D)
- Estrógenos
- SERMs: raloxifeno, bazedoxifeno
- Bisfosfonatos: alendro, risedro, ibandro, zole
- Ranelato estroncio
- Denosumab (anti-RANKL)

Anabólicos

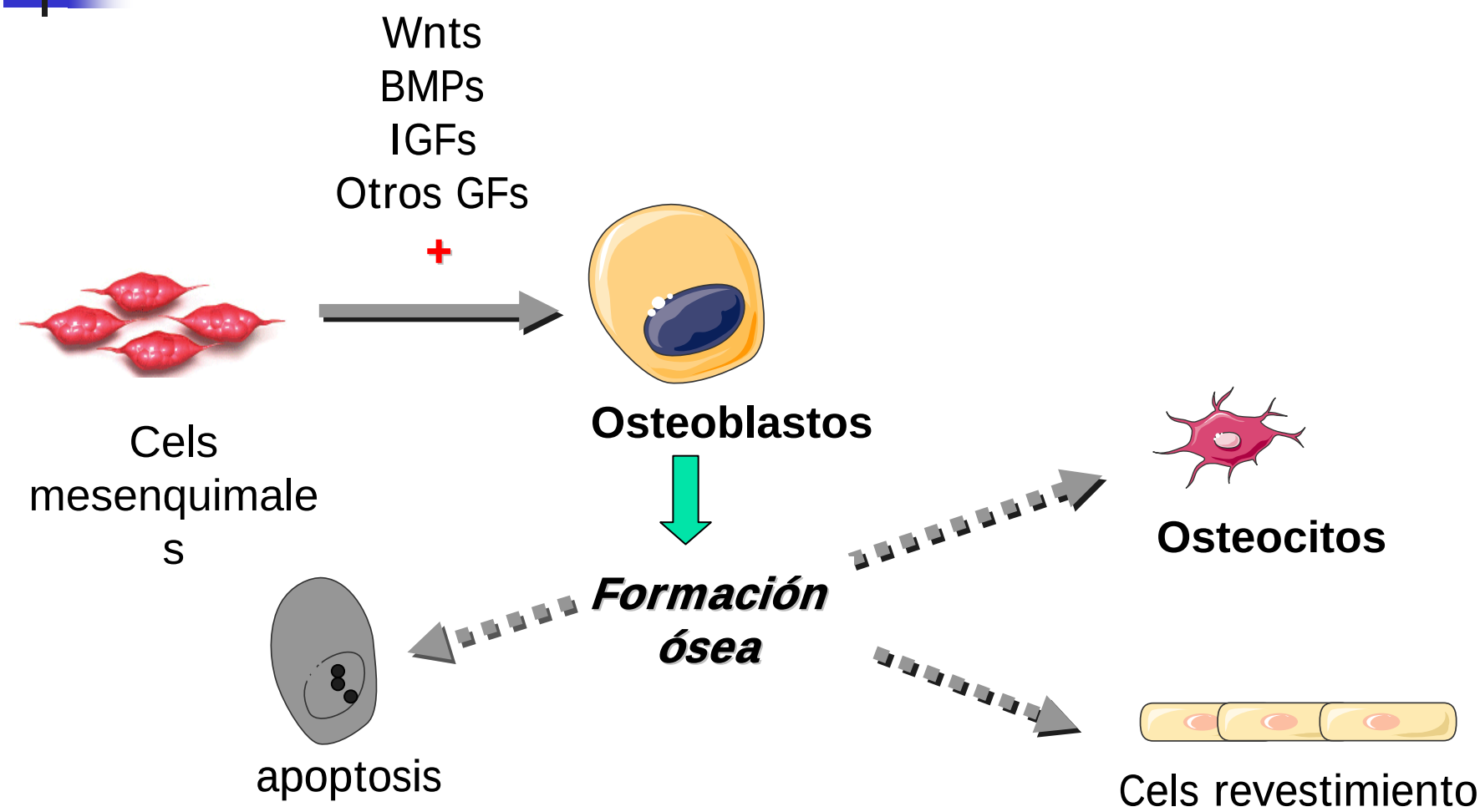
- PTH: teriparatida (1-34), PTH
- Ranelato estroncio?



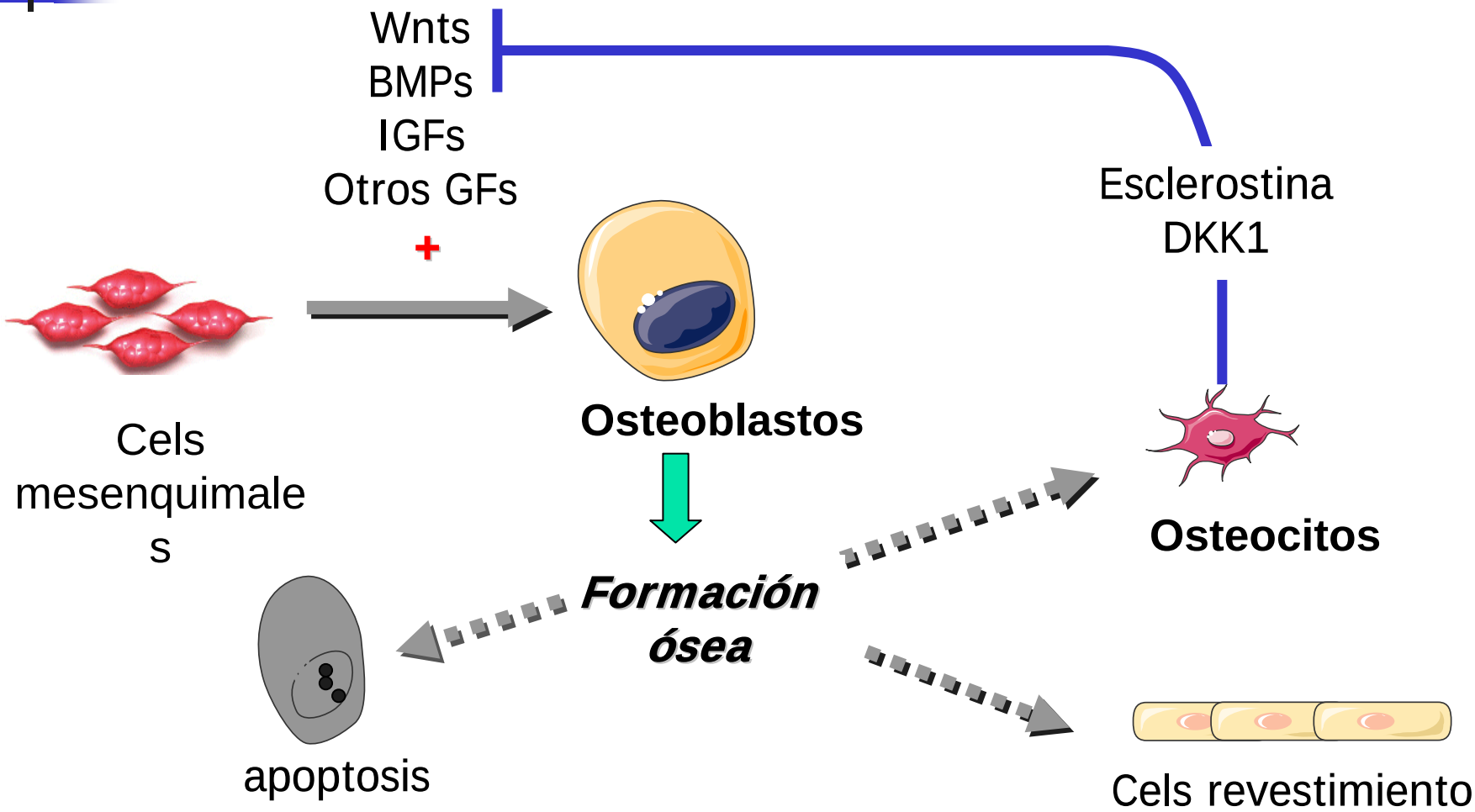
Destino de los osteoblastos



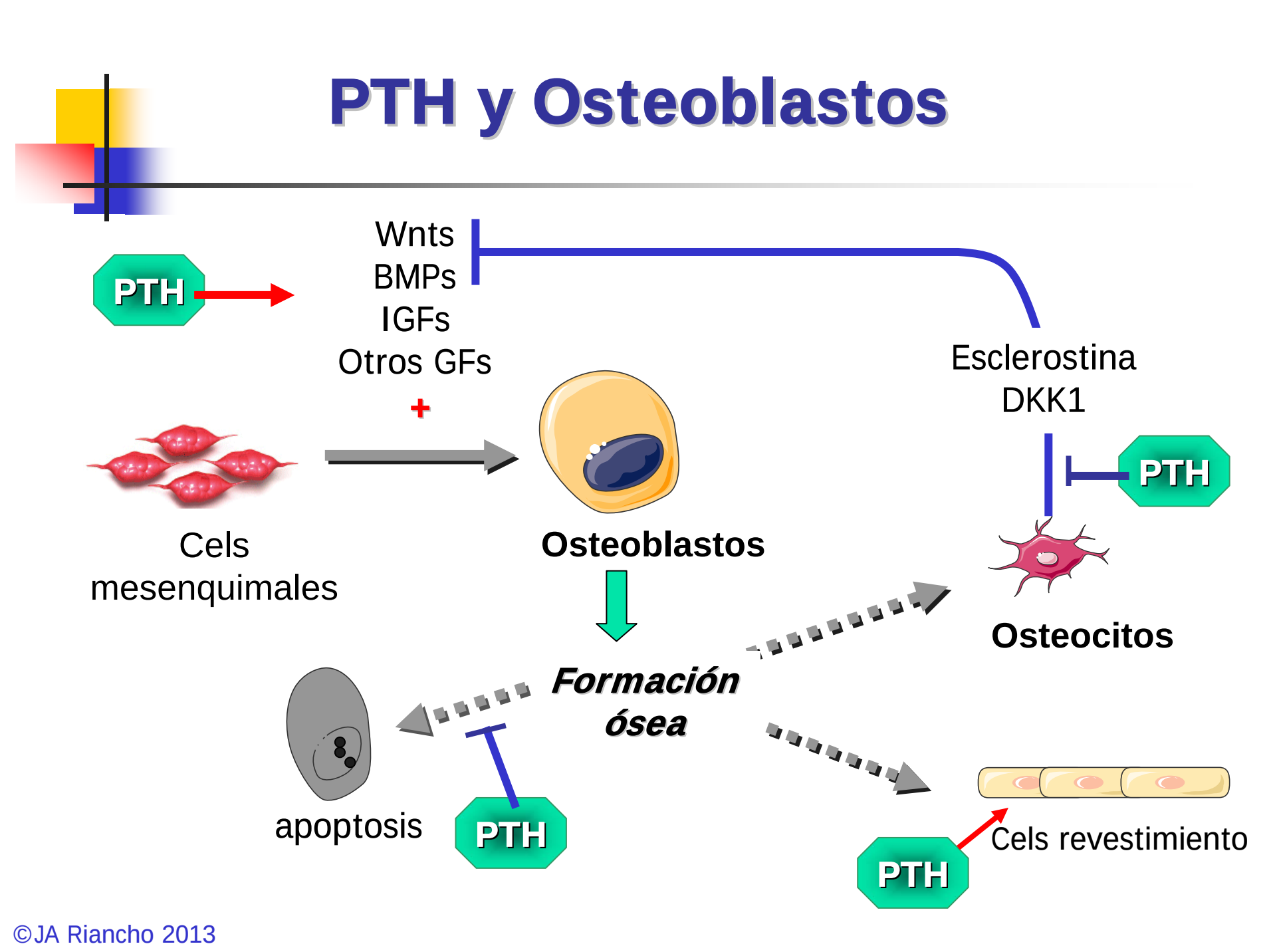
Destino de los osteoblastos



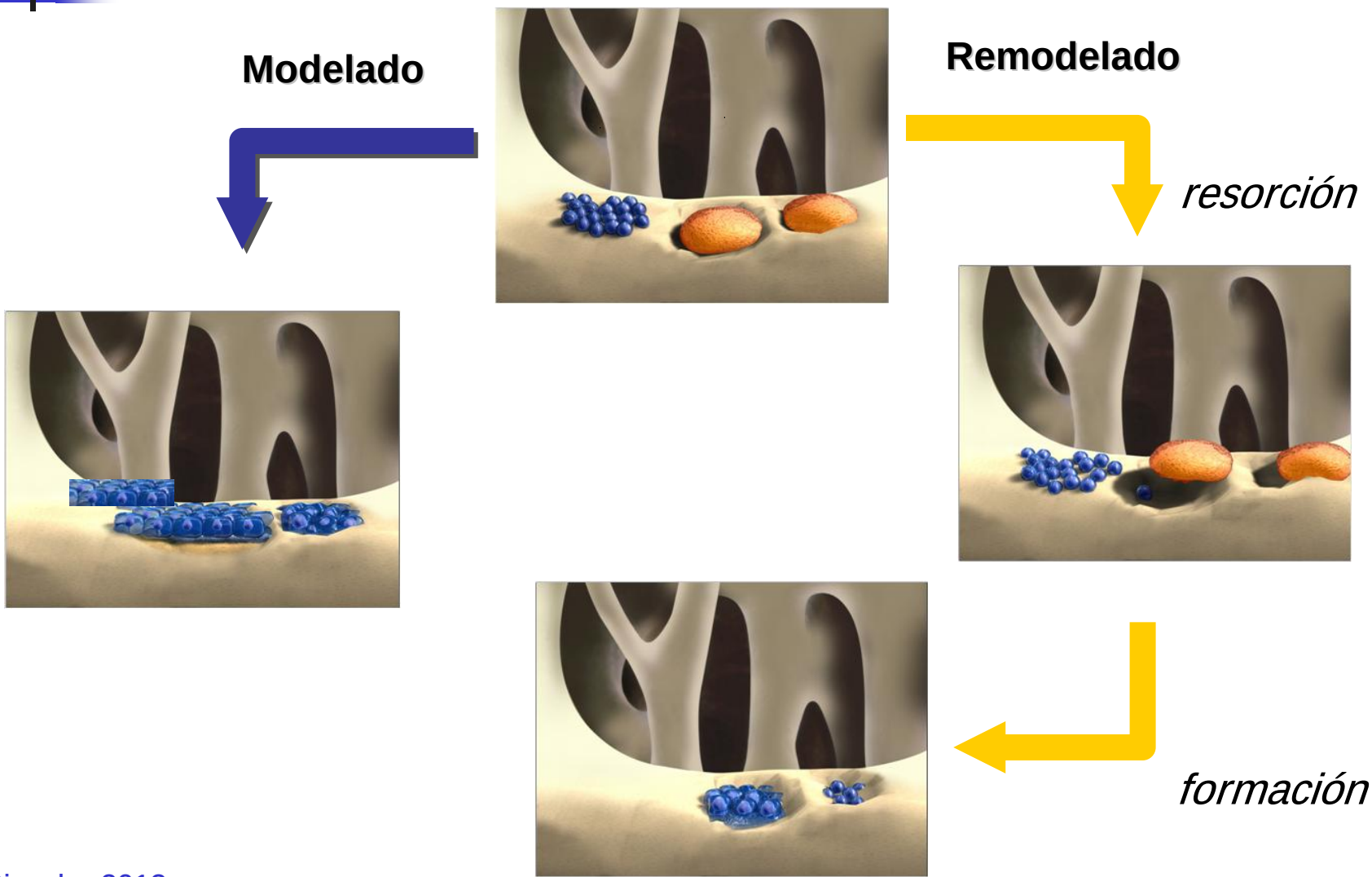
Destino de los osteoblastos



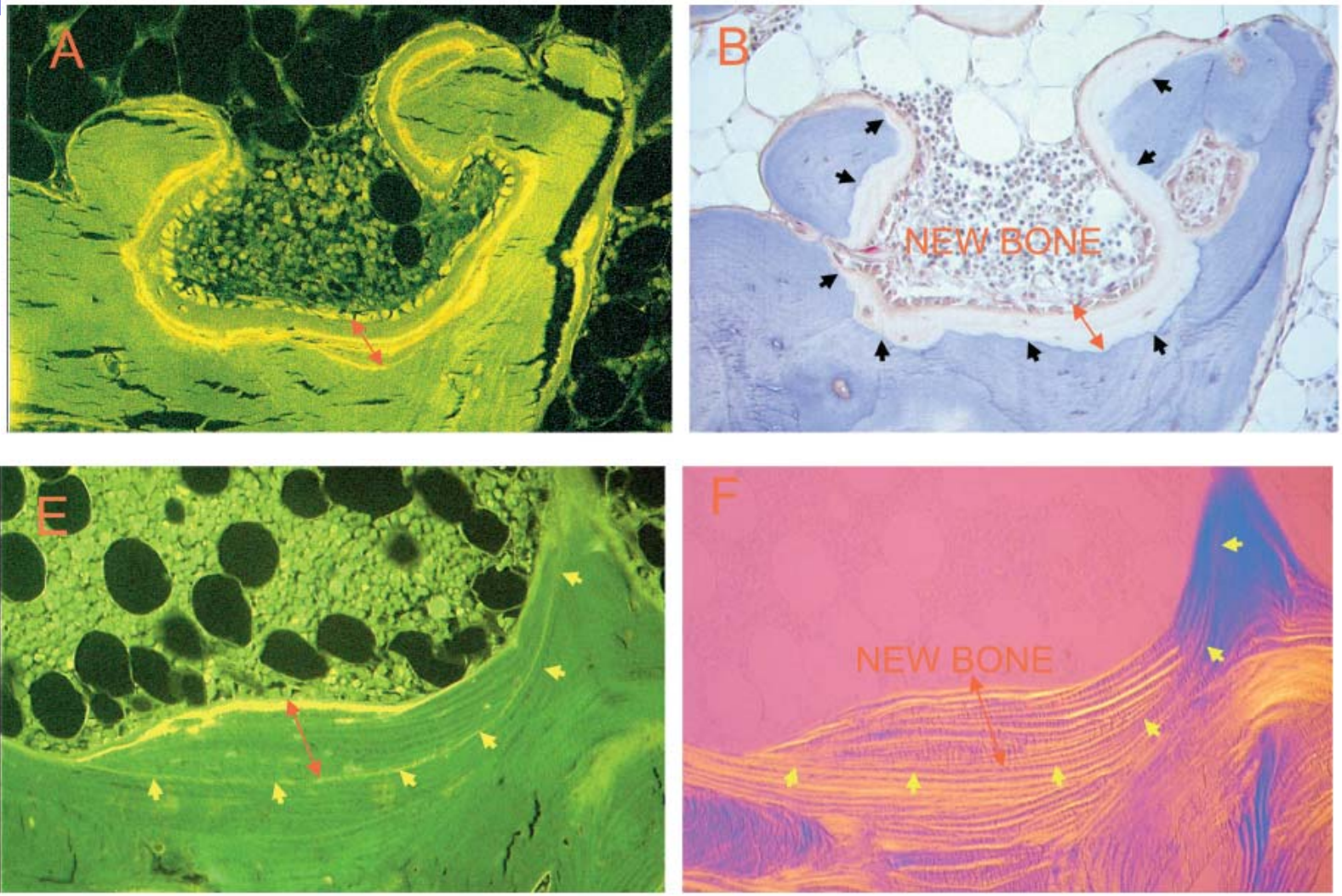
PTH y Osteoblastos



Modelado vs Remodelado



PTH y modelado



Ma, JBMR 2006

Teriparatida y OP PM

TABLE 2. RADIOGRAPHIC EVIDENCE OF NEW VERTEBRAL FRACTURES.*

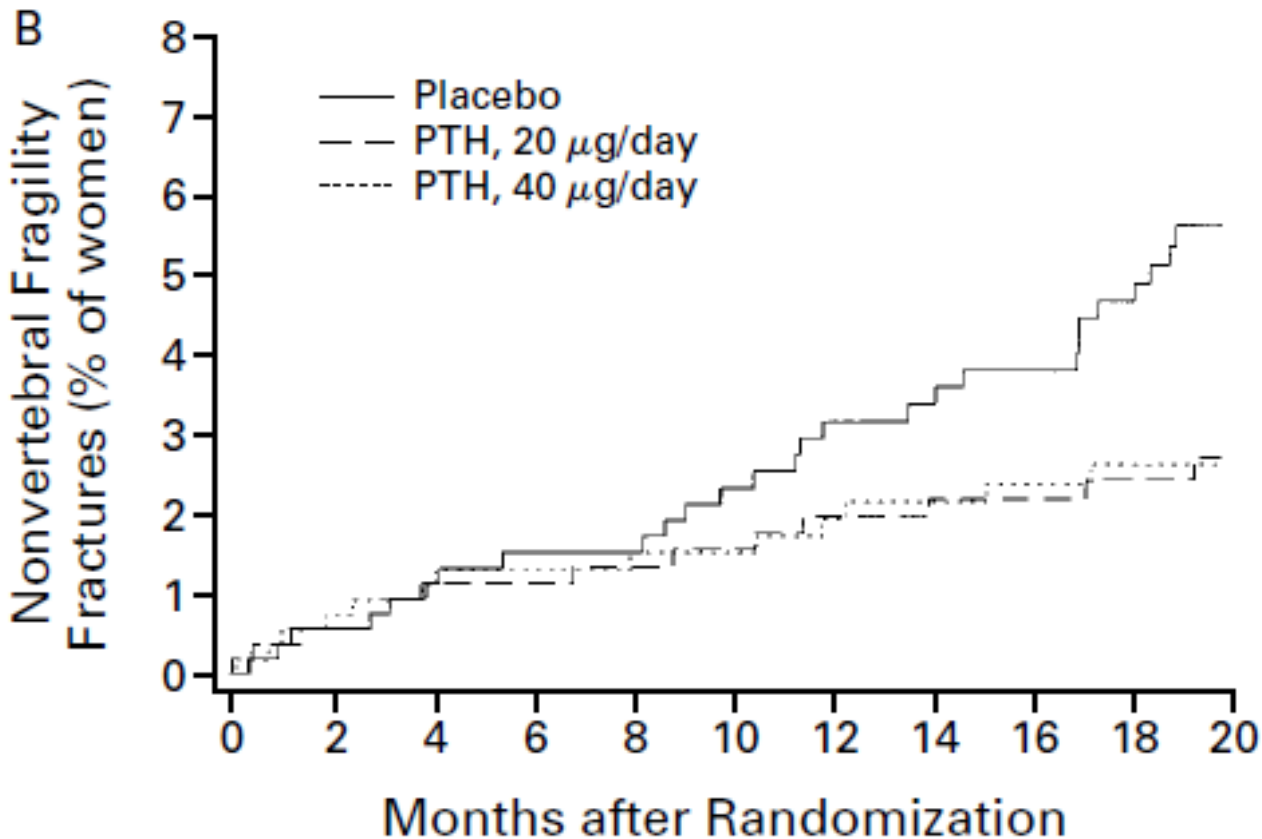
VARIABLE	PLACEBO (N=448)	PTH, 20 μg (N=444)	PTH, 40 μg (N=434)
No. of months at risk (randomization to final radiograph)	21±3	21±3	20±4
≥1 Fracture			
No. of women (%)	64 (14)	22 (5)†	19 (4)†
Relative risk (95% CI) vs. placebo	—	0.35 (0.22–0.55)	0.31 (0.19–0.50)
Percent reduction in absolute risk	—	9	10
>1 Fracture			
No. of women (%)	22 (5)	5 (1)†	3 (<1)†
Relative risk (95% CI) vs. placebo	—	0.23 (0.09–0.60)	0.14 (0.04–0.47)
Percent reduction in absolute risk	—	4	4
≥1 Moderate or severe fracture			
No. of women (%)	42 (9)	4 (<1)†	9 (2)†
Relative risk (95% CI) vs. placebo	—	0.10 (0.04–0.27)	0.22 (0.11–0.45)
Percent reduction in absolute risk	—	9	7

*Plus–minus values are means ±SD. PTH denotes parathyroid hormone (1-34), and CI confidence interval.

†P≤0.001 for the comparison with placebo.

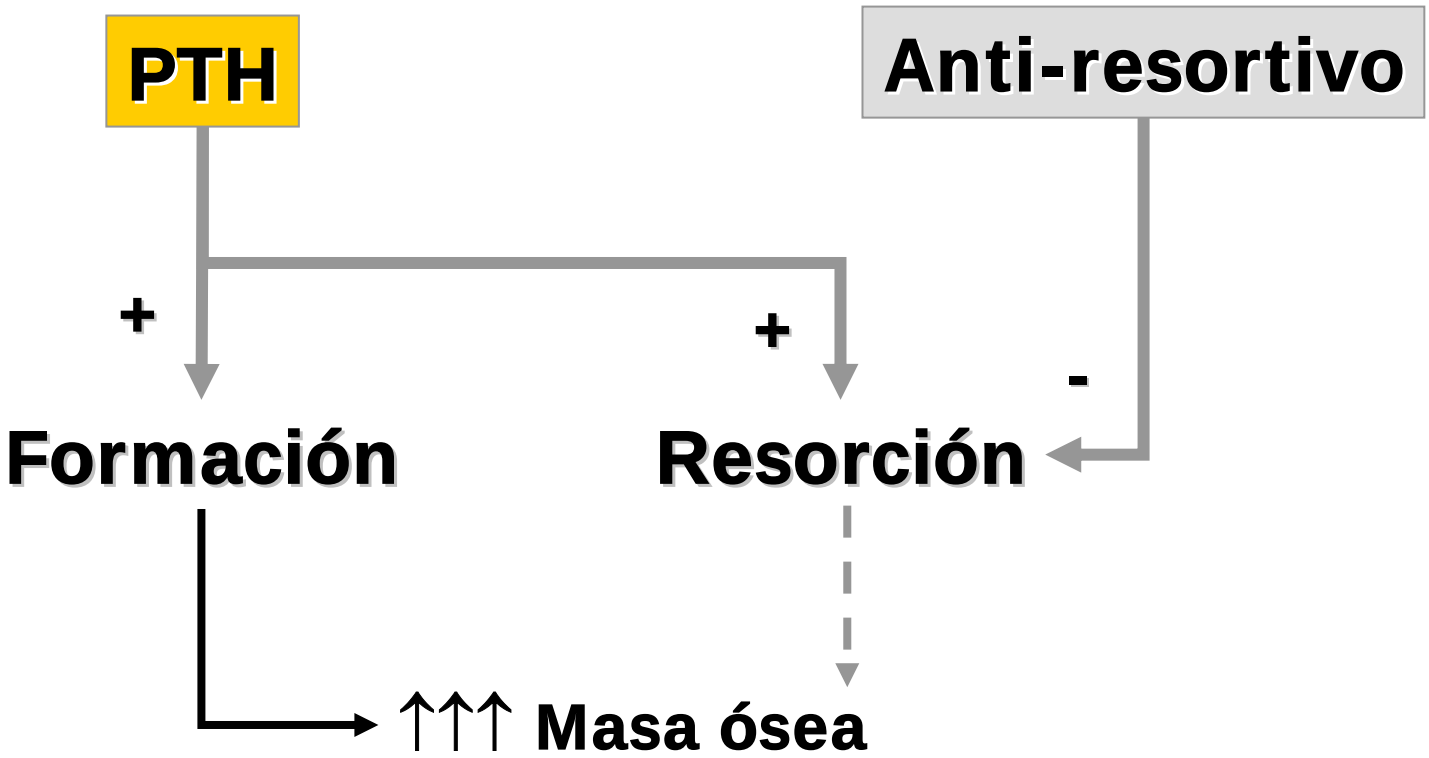
Neer, NEJM 2001

Teriparatida y OP PM



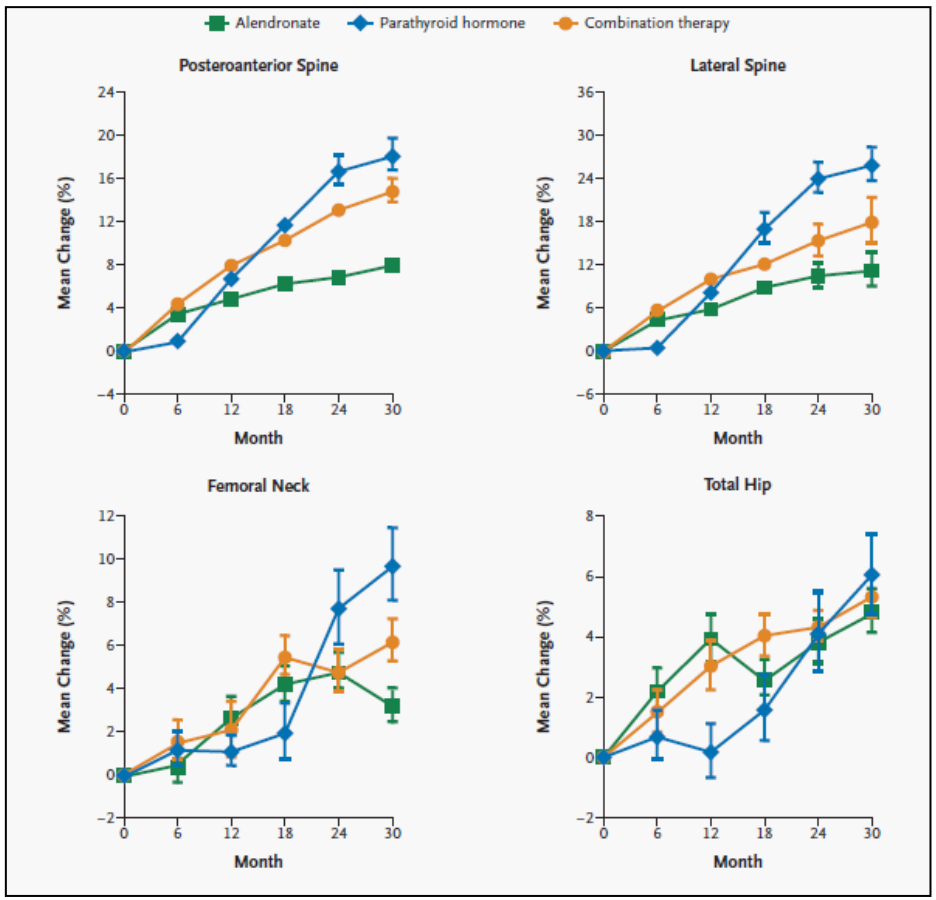
Neer, NEJM 2001

Tto combinado



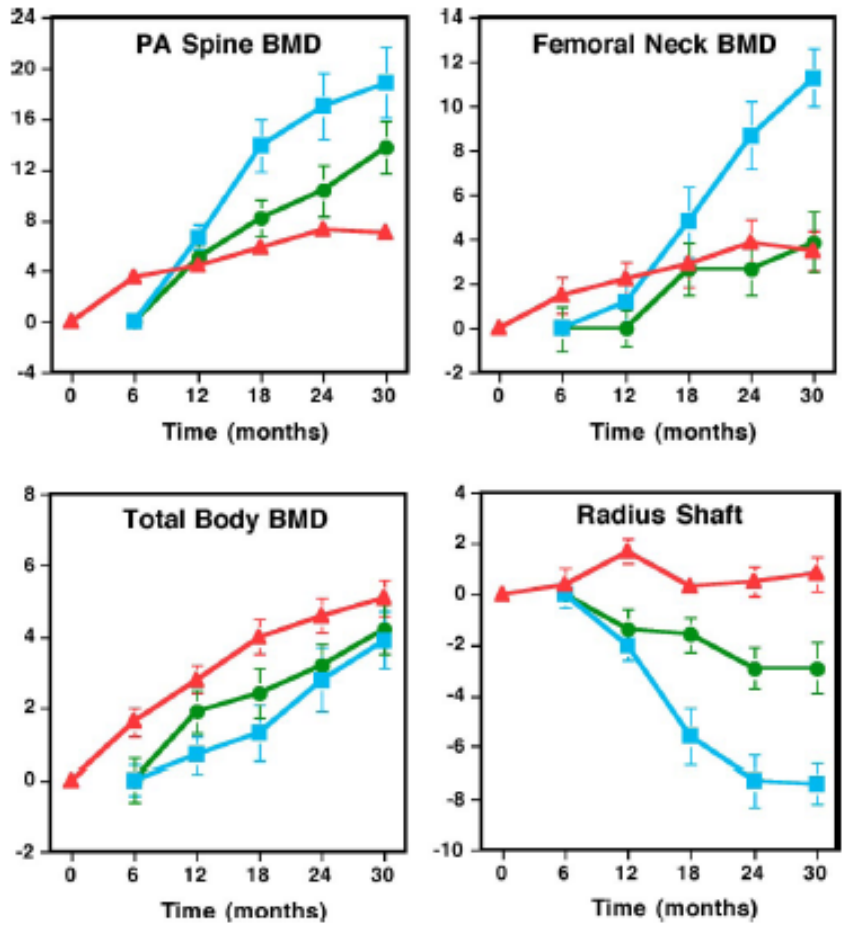
Tto combinado: PTH + ALN

Hombres



Finkelstein NEJM 2003

Mujeres



Finkelstein JCEM 2010

Tto secuencial y combinado

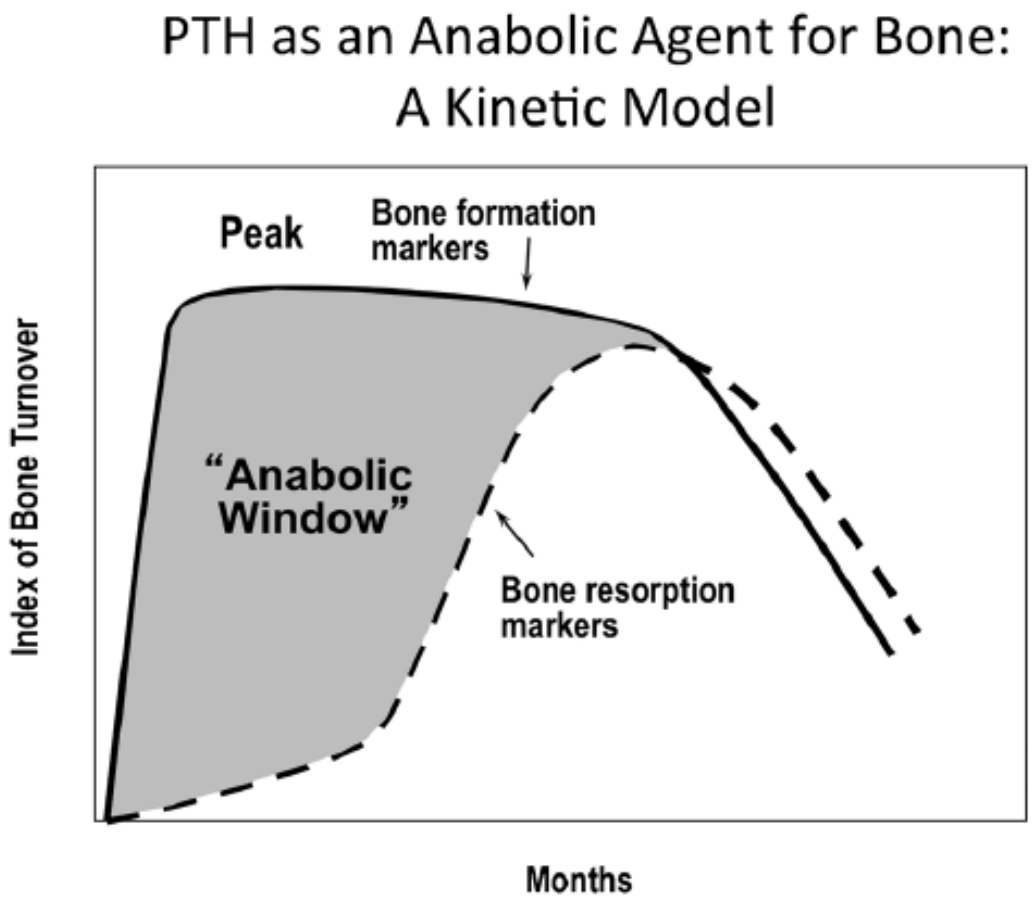
- PTH → Antirresortivo (ALN): 
- PTH + ALN 

Tto secuencial y combinado

- PTH → Antirresortivo (ALN): 
- PTH + ALN 

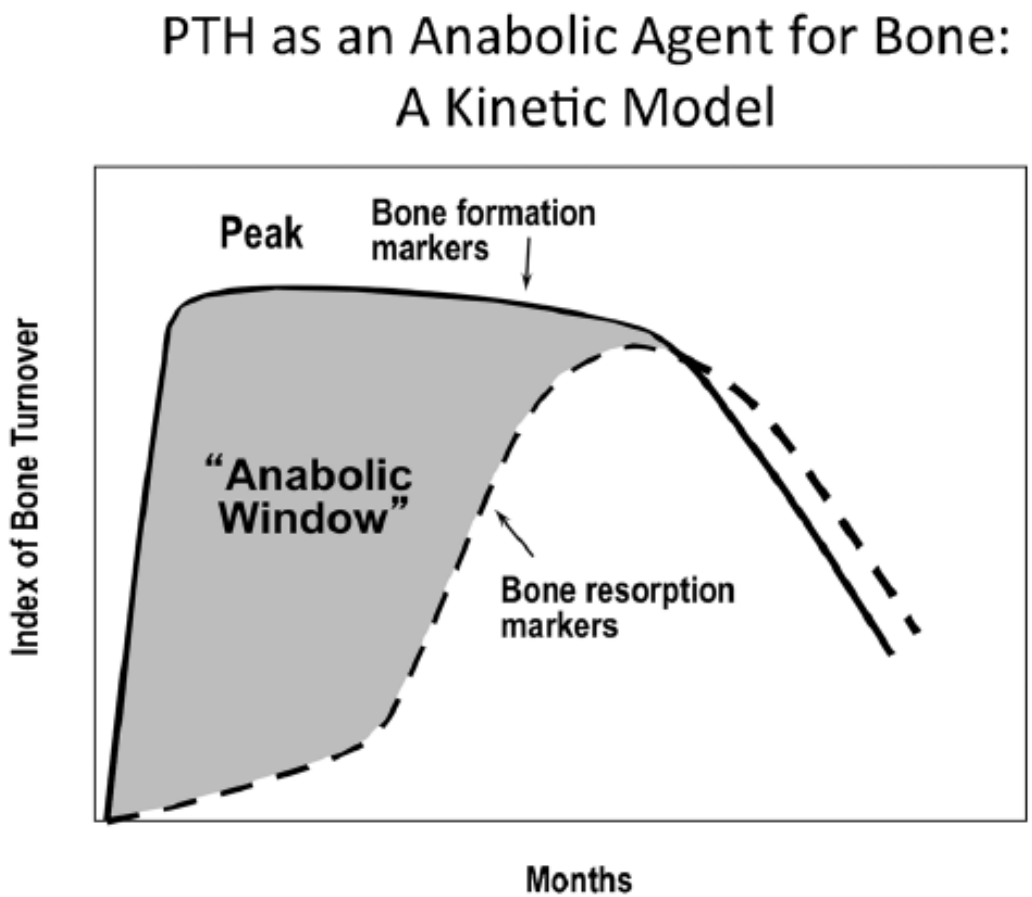
- PTH + RIS  18m, n=29
- PTH + ZOLE  12m
- PTH + RALOX  6m
- PTH + DMAB  12m

La “ventana anabólica”

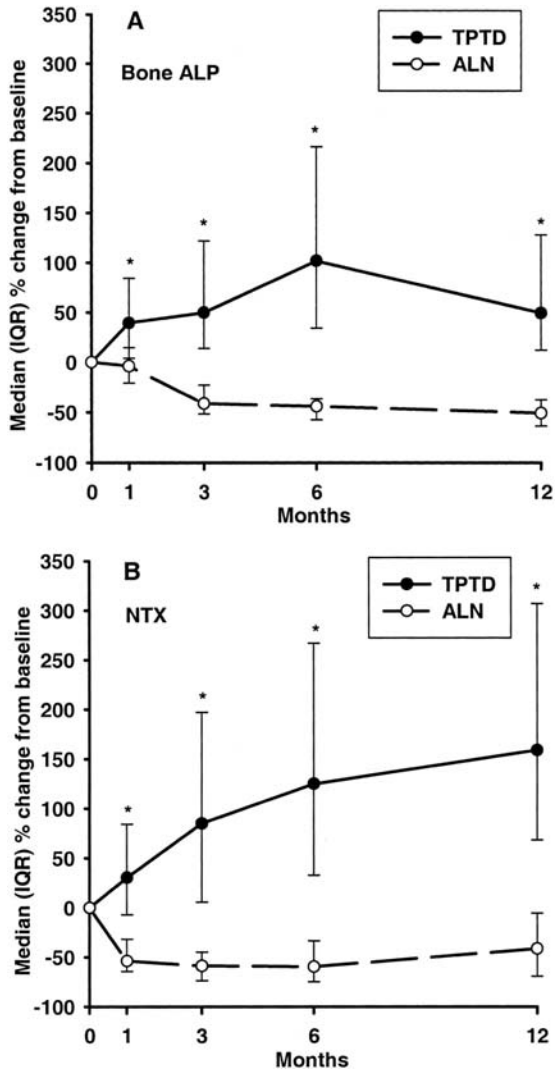


Capriani JBMR 2012

La “ventana anabólica”

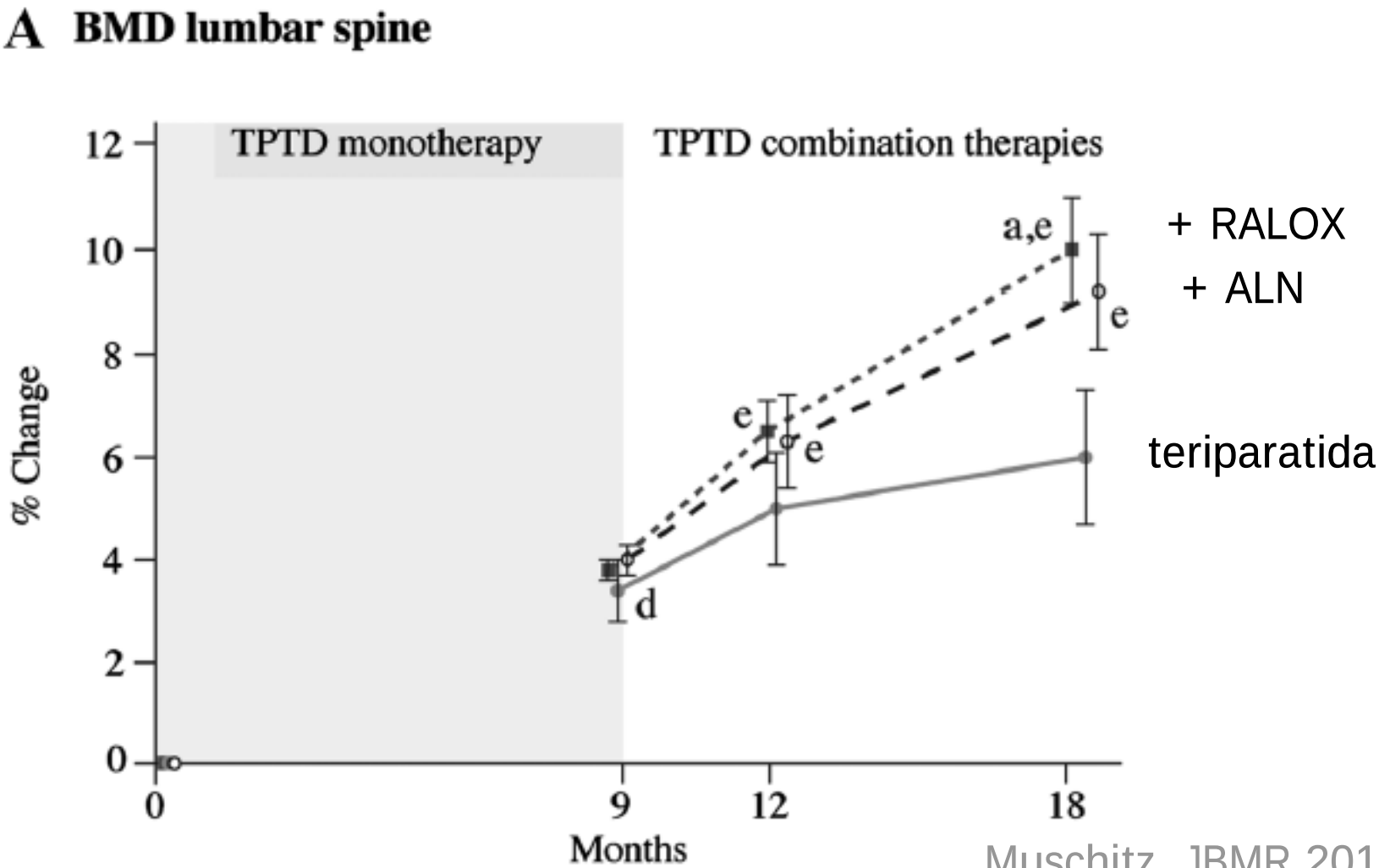


Capriani JBMR 2012



Body JCEM 2002

Tto secuencial acelerado



Muschitz, JBMR 2013

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- (Calcio, vitamina D)
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- **Ranelato estroncio**
- Denosumab (anti-RANKL)

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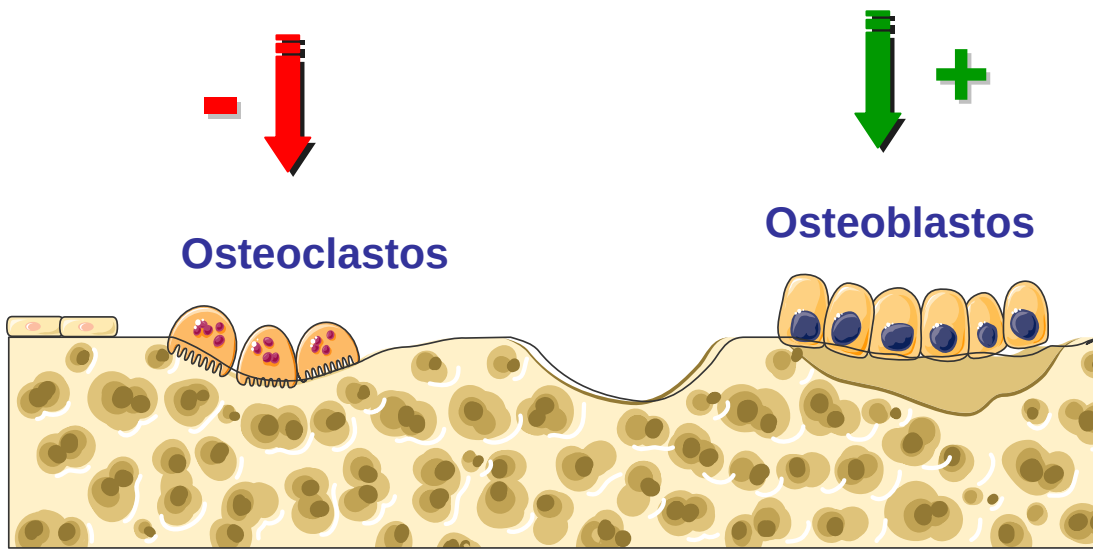
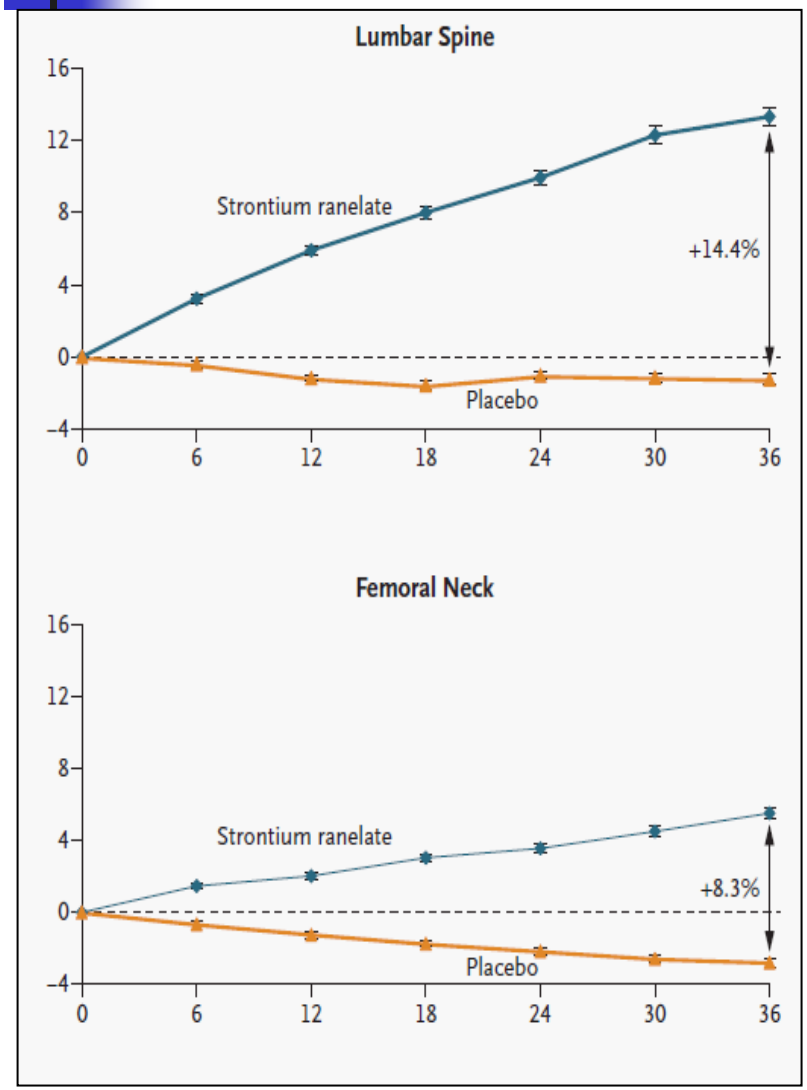
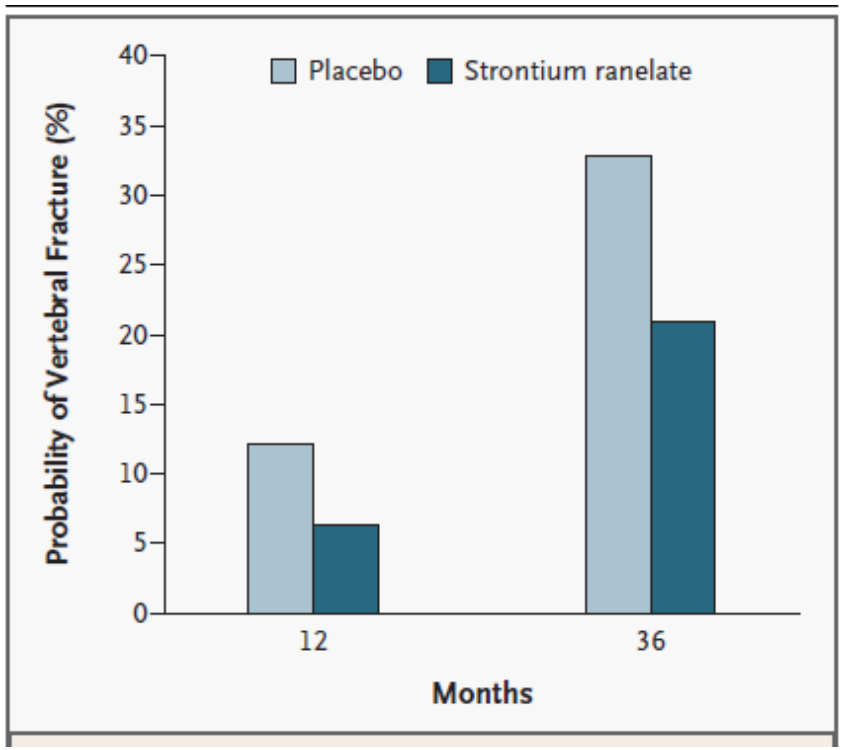
- **Ranelato estroncio?**



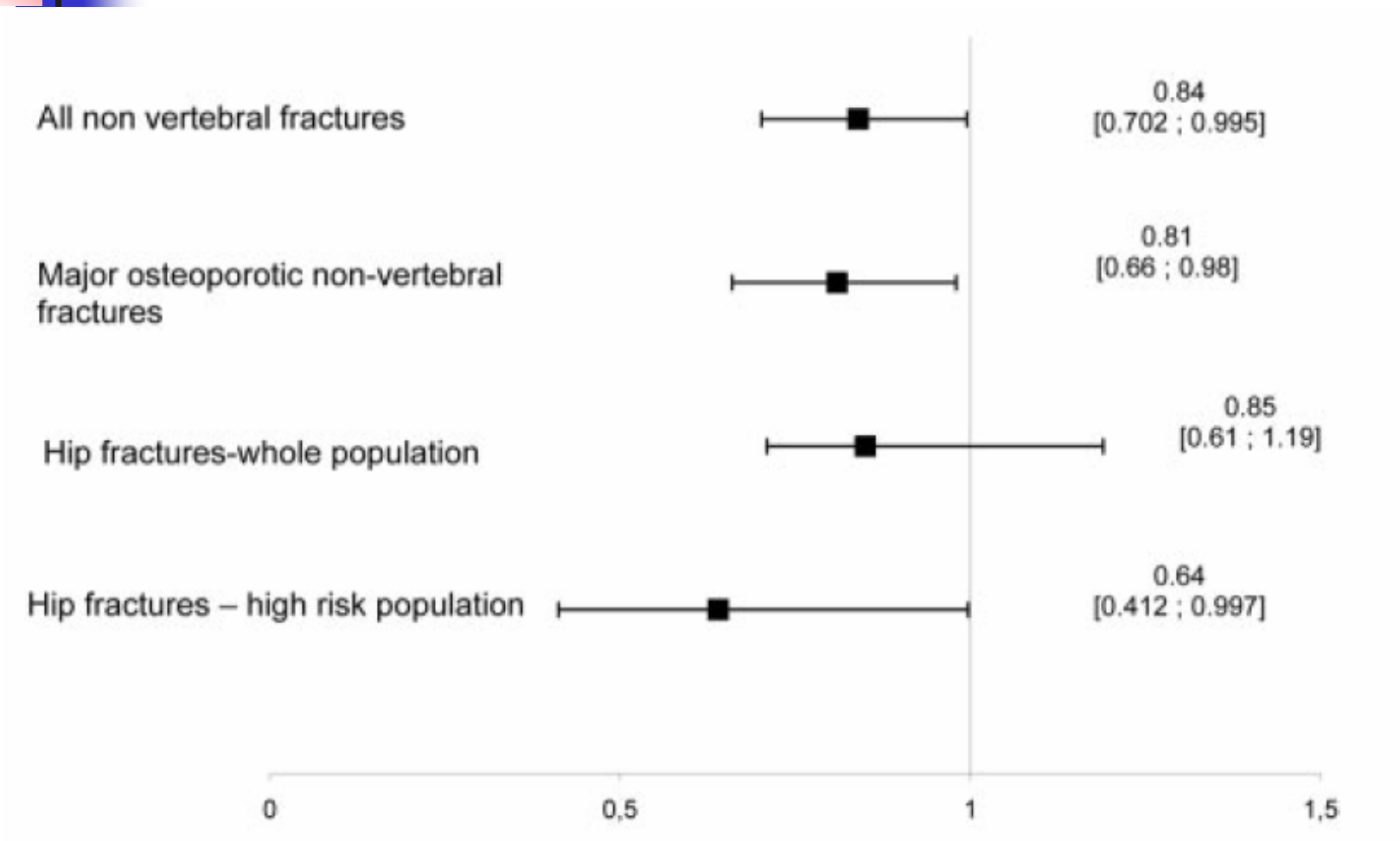
Estroncio y osteoporosis





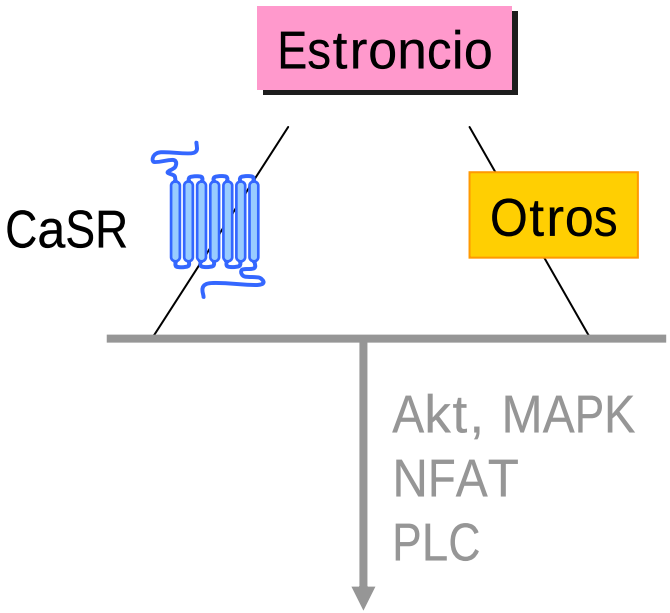
Meunier NEJM 2004

Estroncio y Frx no vertebrales

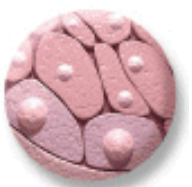


Reginster JCEM 2005

Estroncio: mecanismo acción



Wnts
Esclerostina
FGF



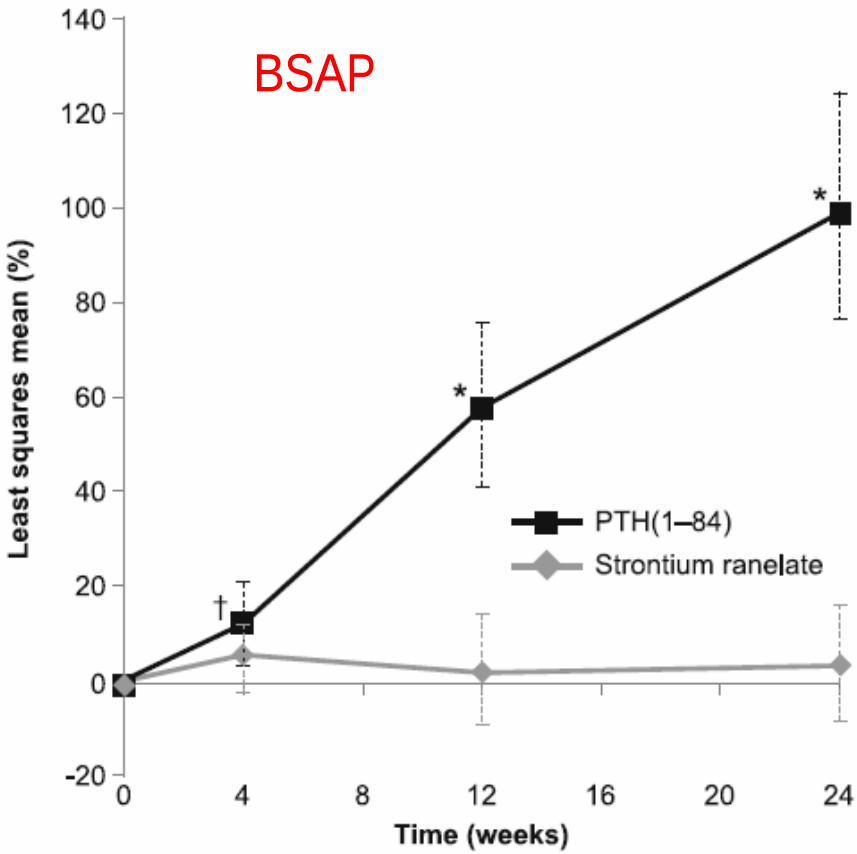
Adipocitos

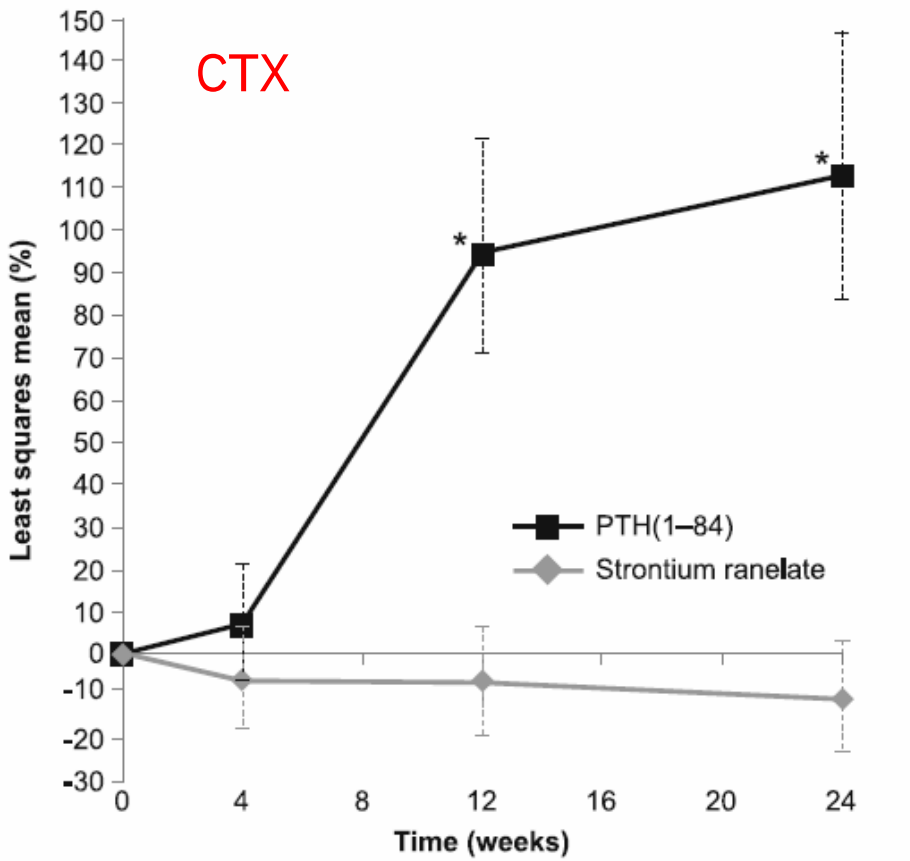
MSCs

Osteoblastos

Proliferación
Diferenciación
↓ Apoptosis

Estroncio *vs* PTH: marcadores



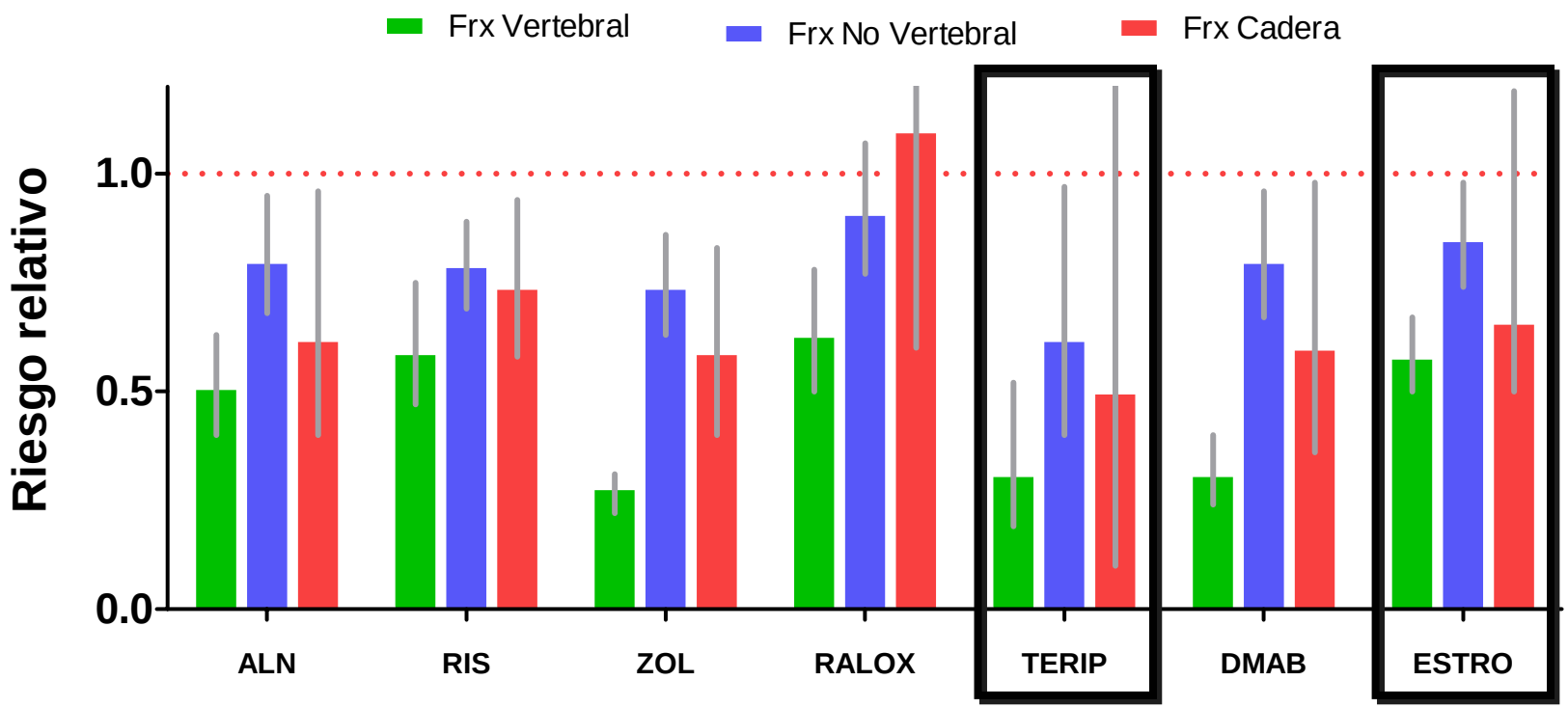


Quesada, OI 2011

Balance positivo

	Resorción	Formación
Bisfosfonatos	↓↓	↓
PTH	↑	↑↑
Estroncio	↓	-↑

Riesgo fractura



Dibujado con datos de Hopkins et al (The relative efficacy of nine osteoporosis medications for reducing the rate of fractures in post-menopausal women. BMC Musculoskeletal Disorders 2011, 12:209)

Evidencia eficacia anti-fractura

Table 3 Effect of major pharmacological interventions on fracture risk when given with calcium and vitamin D in postmenopausal women with osteoporosis

	Vertebral fracture	Non-vertebral fracture	Hip fracture
Alendronate	A	A	A
Ibandronate	A	A[1]	nae
Risedronate	A	A	A
Zoledronate	A	A	A
Denosumab	A	A	A
Raloxifene	A	nae	nae
Strontium ranelate	A	A	A[1]
Teriparatide	A	A	nae

nae: not adequately evaluated
[1]in subsets of patients (post-hoc analysis)

NOS/NOGG (Reino Unido)
http://www.shef.ac.uk/NOGG/

Osteoporos Int (2013) 24:209–217
DOI 10.1007/s00198-012-2068-9

ORIGINAL ARTICLE

Results of indirect and mixed treatment comparison of fracture efficacy for osteoporosis treatments: a meta-analysis

N. Freemantle · C. Cooper · A. Diez-Perez · M. Gitlin · H. Radcliffe · S. Shepherd · C. Roux

Results Using data from 34 studies, random effects meta-analysis showed that all agents except etidronate significantly reduced the risk of new vertebral fractures compared with placebo; denosumab, risedronate, and zoledronic acid significantly reduced the risk for nonvertebral and hip fracture, while alendronate, strontium ranelate, and teriparatide significantly reduced the risk for nonvertebral fractures. MTC

Efectos adversos

PTH: efectos adversos

- Cefalea, gastrointestinales: 8-25%
- Hipercalciuria: 5-10%
- Hipercalcemia: 0-10%
- Hiperuricemia: 3%
- Osteosarcoma: no (3 casos/ $1x10^6$ pacientes)
- Embarazo/lactancia: evitar (FDA C: no datos)
- Historia cáncer: evitar*

Cipriani, JBMR 2012

Estroncio: efectos adversos

- Gastrointestinales: 5-15 %
- Trombosis venosa/TEP: 0,2-0,03 %
  - Evitar si antecedentes o factores riesgo
  - Reconsiderar si >80 años (EMA Marzo-2012)
- Infarto de miocardio
  - Evitar si antecedentes de cardiopatía isquémica, ACVA, isquemia periférica o HTA (EMA Abril-2013)
- Cutáneos: 1-3% (DRESS 0,1%)
- Embarazo/lactancia: evitar (no datos)

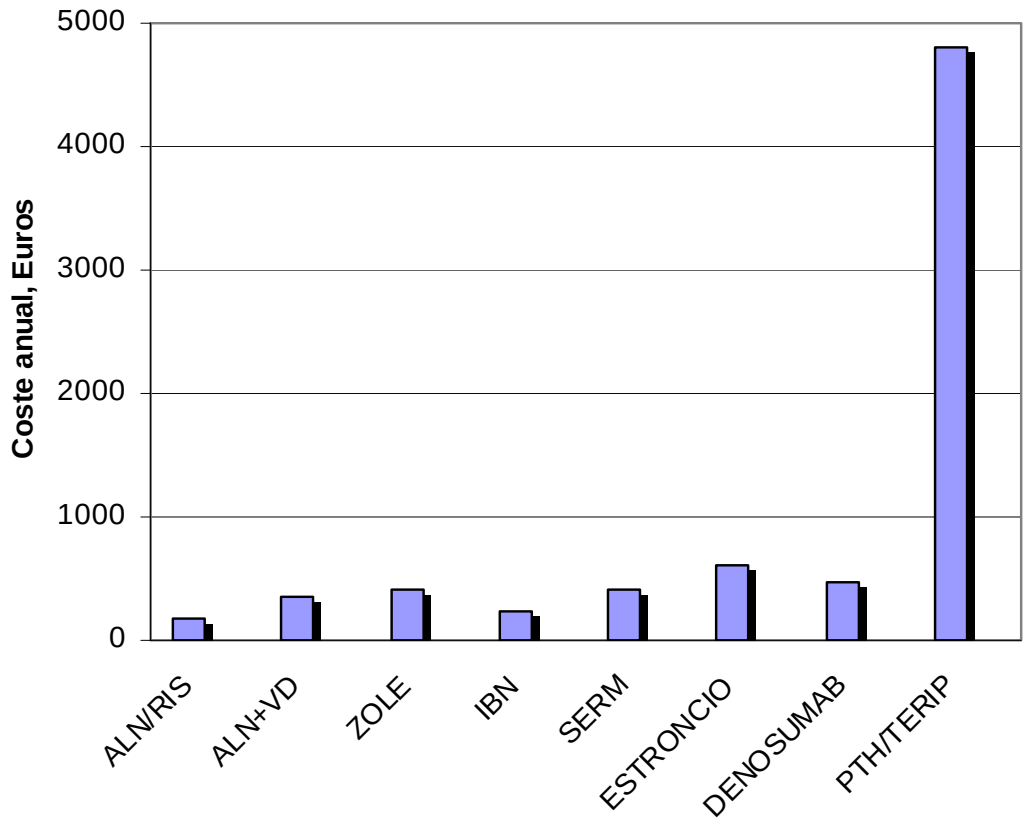
Jonville-Bera Press Med 2011; Reginster OI 2012

Coste del tratamiento

Coste mensual aprox (Euros):

- ALN, RIS: 15-30 (± vit D)
- Zole: 30
- IBN: 20
- SERM: 35
- Denosumab: 40
- Ranelato estroncio: 50

- **PTH/teriparatida: 400**



En conclusión . . .

- **PTH:** potente efecto anabólico, ↑DMO y ↓ frx vertebrales y no vertebrales (¿cadera?), estando en el grupo de fármacos más potentes, junto a Zole y Dmab. Coste es 10-20 veces superior al de otros fármacos anti-osteoporóticos.

- La efectividad de las **pautas combinadas** (PTH + antirresortivos) no es bien conocida, pero debe evitarse la administración simultánea de PTH+ALN.

- **Estroncio** parece tener un efecto doble, ↑ DMO (en parte falsamente) y ↓ frx vertebrales y no vertebrales (¿cadera?). Coste algo superior al de otros fármacos. Puede tener efectos secundarios graves.