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ITALIAN CHAPTER
16° Congresso Nazionale AME
Joint Meeting with AACE Italian Chapter
ITALIAN CHAPTER

Guida all'iperparatiroidismo

Trattamento non chirurgico

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Conflitti di interesse

Ai sensi dell'art. 3.3 sul conflitto di interessi, pag 17 del Regolamento Applicativo Stato-Regioni del 5/11/2009, dichiaro che negli ultimi 2 anni ho avuto rapporti diretti di finanziamento con i seguenti soggetti portatori di interessi commerciali in campo sanitario:

- SHIRE

- Abiogen Pharma

Trattamento non chirurgico

Observation

Calcium and Vitamin D supplementation

Medical management

- Antiresorptive drugs
  - Estrogens (SERMS)
  - Bisphosphonates
- Calcimimetics

Other options

- Percutaneous ethanol injection
- Percutaneous laser ablation
- High intensity focused ultrasounds

Trattamento non chirurgico

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- Calcimimetics

Other options

- Percutaneous ethanol injection
- Percutaneous laser ablation
- High intensity focused ultrasounds

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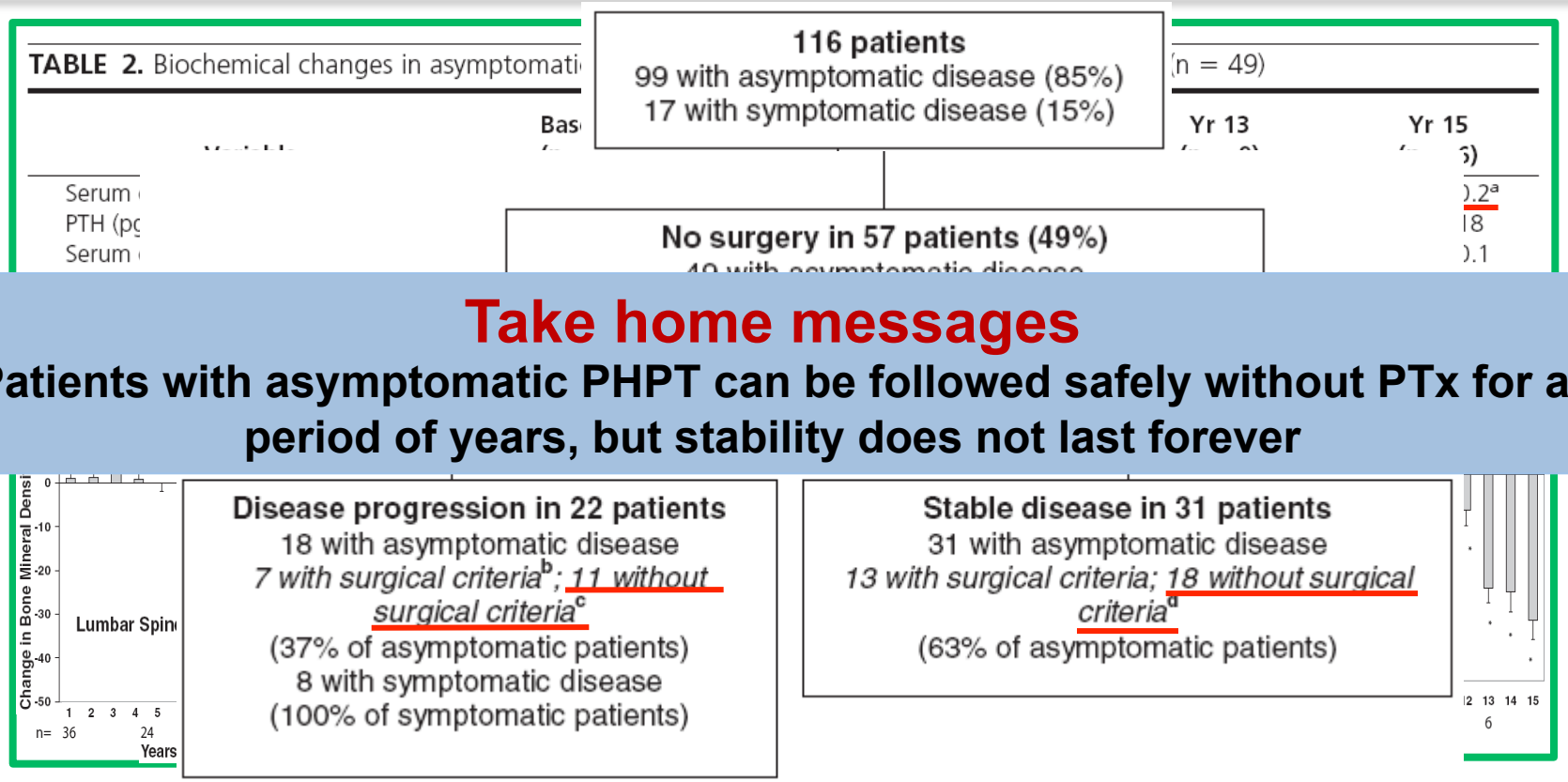

Take home messages

Patients with asymptomatic PHPT can be followed safely without PTx for a period of years, but stability does not last forever

Rubin et al. JCEM 2008

Trattamento non chirurgico

Observation

Calcium and Vitamin D supplementation

Medical management options

- Antiresorptive drugs
  - Estrogens (SERMS)
  - Bisphosphonates
- Calcimimetics

Trattamento non chirurgico

Calcium and vitamin D

SIE: position statement

J Endocrinol Invest (2015) 38:577–593

- **32. We recommend** an intake of calcium appropriate for the age and sex as in the general population (1 ØØOO).
- **33. We recommend against** restriction of dietary calcium intake (1 ØØOO).
- **34. We recommend** correcting vitamin D deficiency in all patients with PHPT. Schedule using a daily dose of 800–1000 IU of vitamin D (weekly or monthly doses calculated on this daily dose) should be adopted (1 ØØOO).
- **35. We recommend** increasing serum 25OHD values at >20 ng/mL and to aim to the target established for the general population (1 ØØOO).

International Guidelines

J Clin Endocrinol Metab, October 2014, 99(10):3607–3618

The goal of cautiously administered repletion regimens should be to increase the serum 25OHD levels to >50 and up to 75 nmol/L.

AME position statement: Primary hyperparathyroidism in clinical practice

J Endocrinol Invest 2012

Vitamin D supplementation in vitamin D deficient patients with PHPT, as currently done for non-PHPT patients

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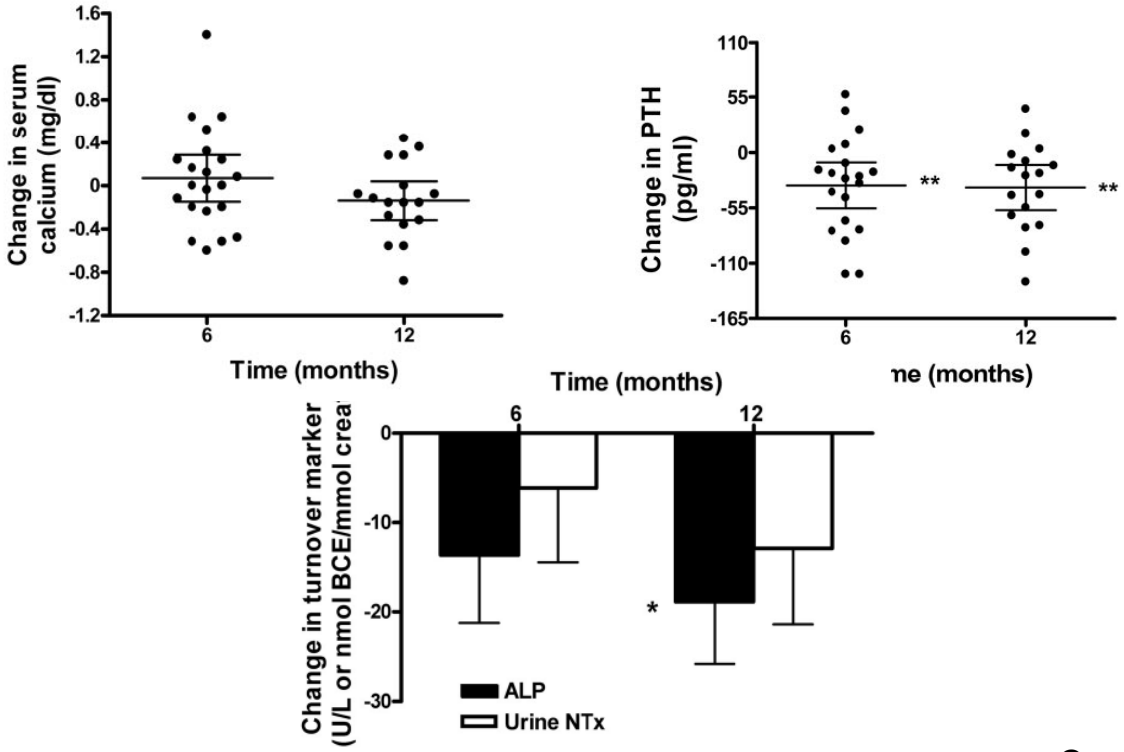
50.000 IU D_2 /week for 1 month and then monthly



Grey et al. JCEM 2005

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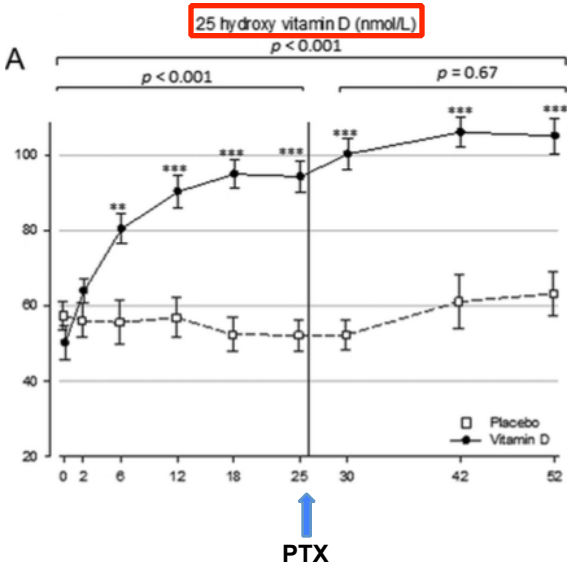
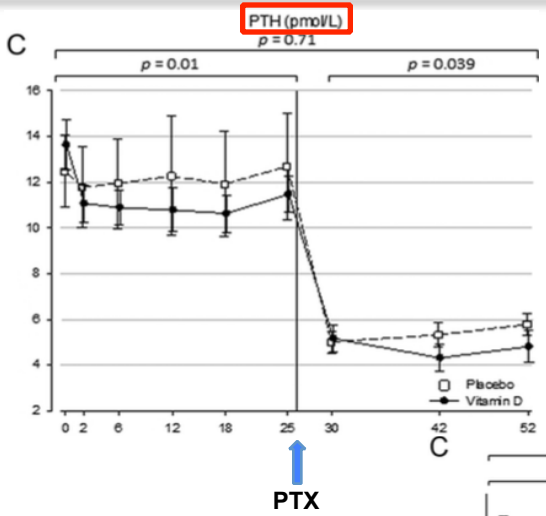
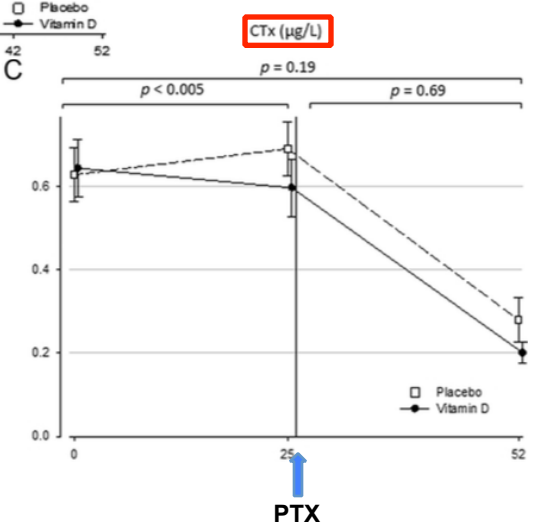
- **46 patients with PHPT who were eligible for PTx . Randomized to receive either daily 2800IU Vit D3 or placebo**







Rolighed et al. JCEM 2014

Trattamento non chirurgico

Observation

Calcium and Vitamin D supplementation

Medical management options

- Antiresorptive drugs
  - Estrogens (SERMS)
  - Bisphosphonates
- Calcimimetics

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Indications for a non-surgical (medical) approach

- Metastatic parathyroid cancer
- Patients with contraindication to surgery
- Patients with complication of previous neck surgery
- Patients unwilling to undergo surgery
- Failed parathyroidectomy
- Selected asymptomatic patients who met surgical criteria for PTX

Trattamento non chirurgico

Estrogens

Take home messages

- Limited data suggest that therapy with estrogen in patients with PHPT may reduce bone resorption and improve BMD
- Useful option for those unable or unwilling to PTX (especially in the presence of menopausal symptoms).
- The risk-benefit ratio must be evaluated in the individual patient with respect to known relative or absolute contraindications

Marcocci et al. JCEM 2014

Orr-Walker et al. Arch Intern Med 2005

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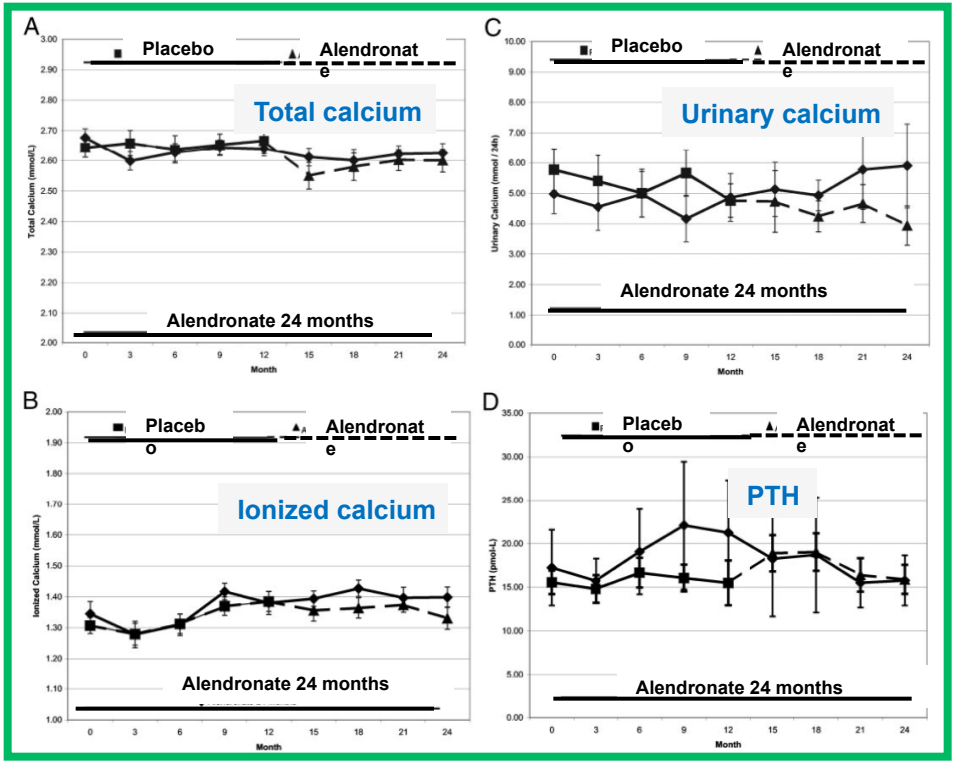
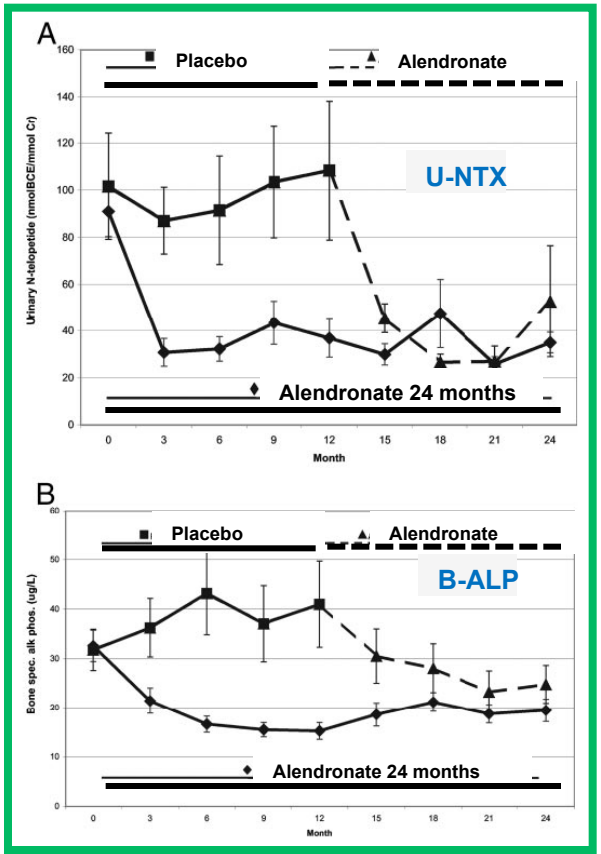
Alendronate

Forty-four patients randomized to alendronate (10 mg daily) or to placebo
Two-year study



Khan et al. JCEM 2004



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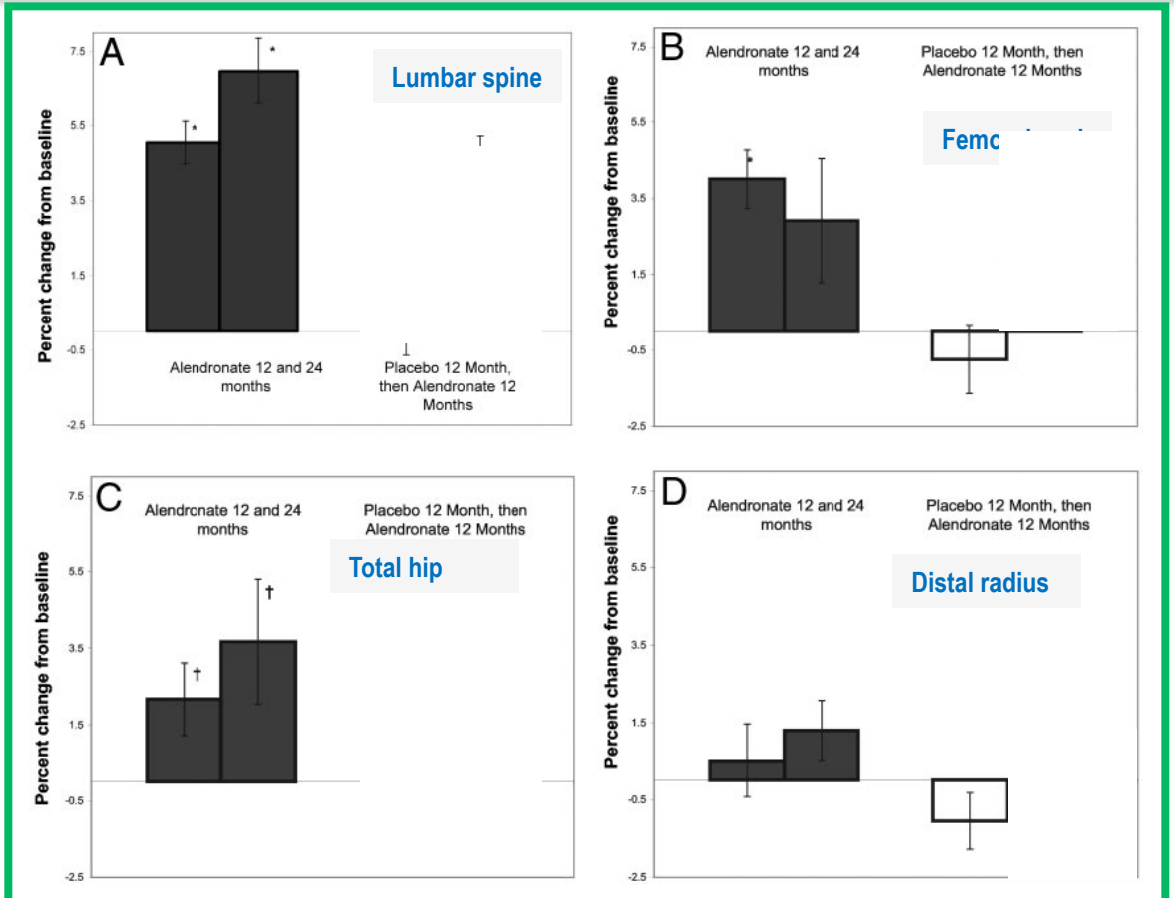


Khan et al. JCEM 2004

Skeletal Effects of Interventions in Mild Primary Hyperparathyroidism: A Meta-Analysis

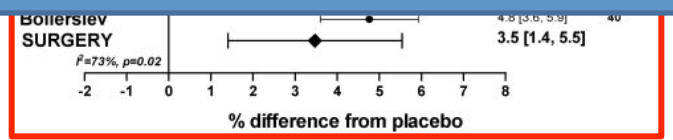
Shyam Sankaran,* Greg Gamble,* Mark Bolland, Ian R. Reid, and Andrew Grey

BMD changes after 1 year in 8 RCT of mild PHPT

Take home messages

- Positive effect of alendronate on BMD at the lumbar spine and hip
- Bone turnover markers decrease with alendronate therapy
- Serum calcium remains stable

In subjects who are not candidates for PTX with low BMD alendronate provides skeletal protection and is a medical option



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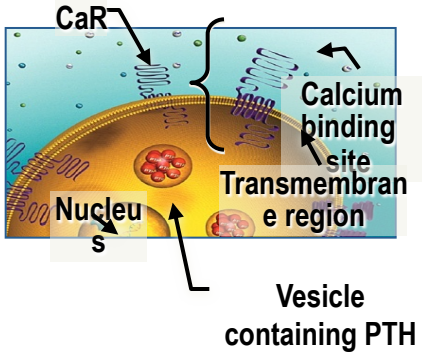
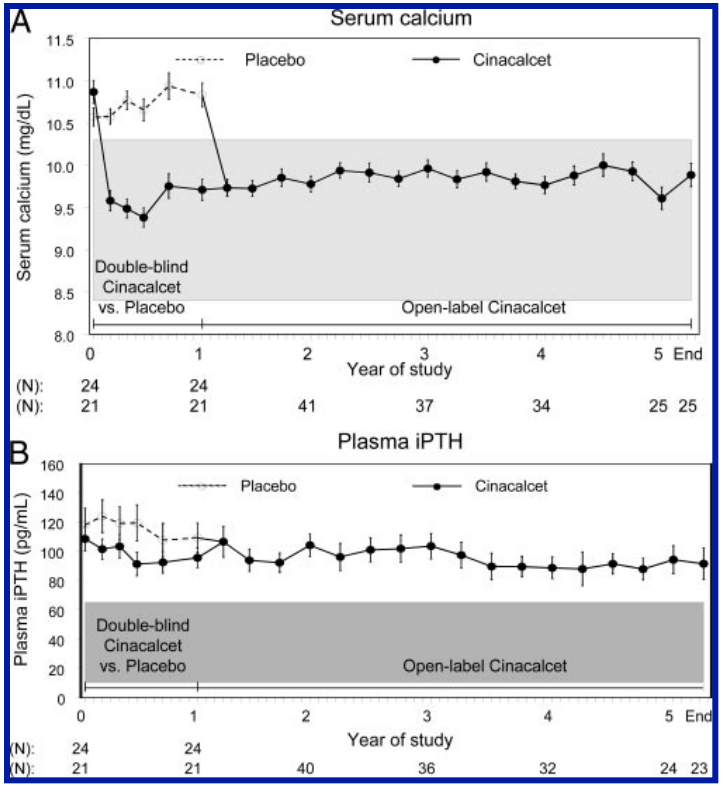
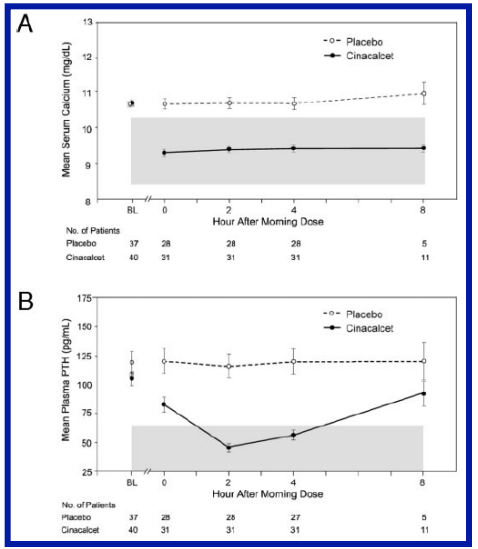
Cinacalcet







Peacock et al. JCEM 2009

Trattamento non chirurgico

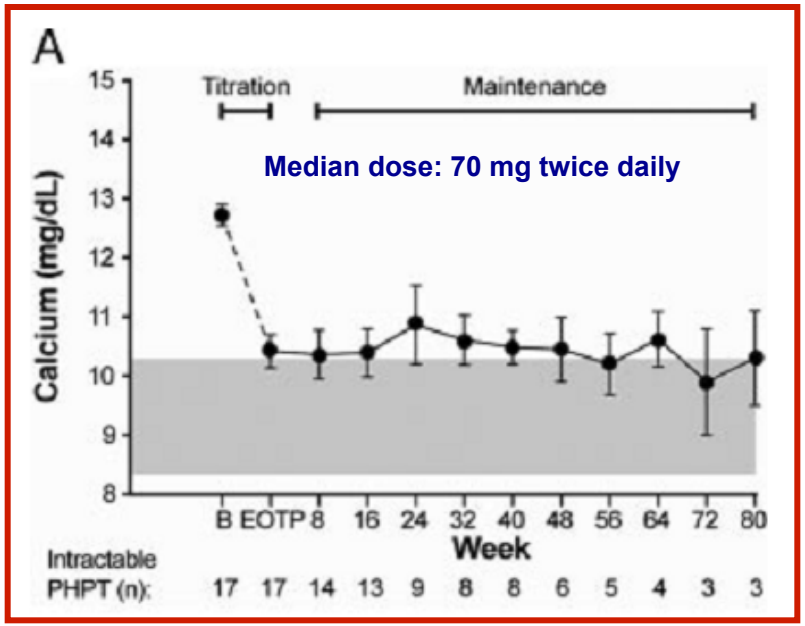
Cinacalcet

TABLE 1. Demographic and baseline characteristics of patients (n = 17)

Baseline parameter	Mean ± SD (range)[a]
Age, yr	65.7 ± 9.0 (52.0–88.0)
Gender: male/female, n	8/9
Race: white/black, n	16/1
Prior parathyroid surgery, n	14
Kidney stone history, n	7
Prior bisphosphonate use, n	10
Serum calcium, mg/dl	12.7 ± 0.8 (11.8–14.5)[b] [3.2 ± 0.2 (3.0–3.6) mmol/liter]
Plasma iPTH, pg/ml	243 ± 105 (100–499) [25.8 ± 11.1 (10.6–52.9) pmol/liter]

[a] Unless otherwise indicated.

[b] Values less than 12.5 mg/dl (3.1 mmol/liter) were due to variation between screening and baseline values.



Marcocci et al., JCEM 2009

Trattamento non chirurgico

TABLE 1. Baseline demographics of parathyroid carcinoma

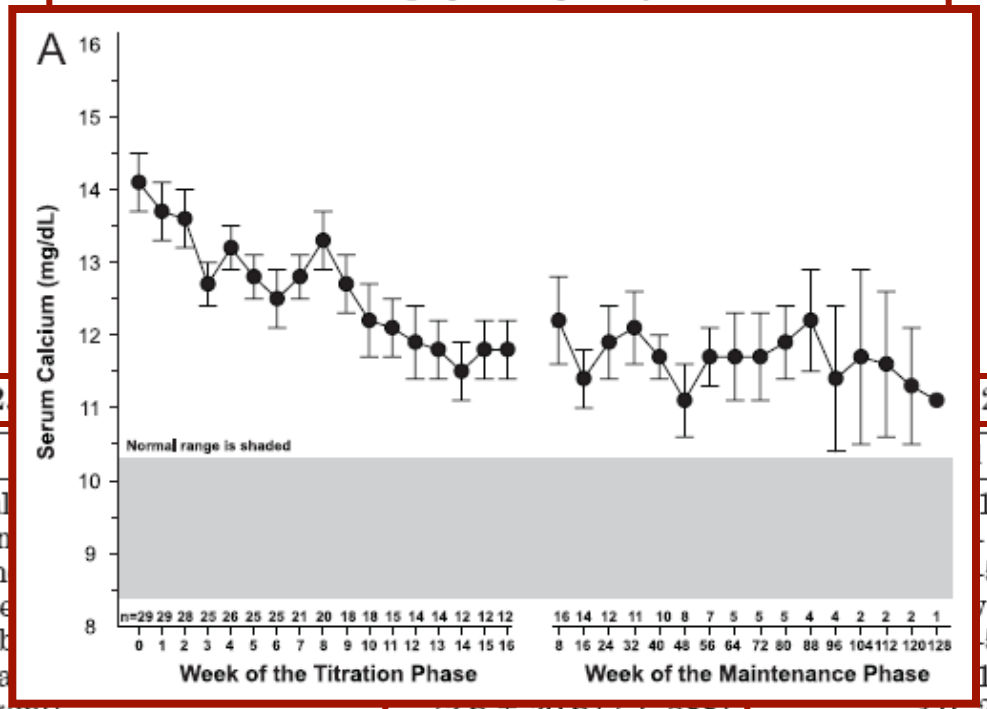


TABLE 2 (29)

		range
Serum cal		10.3
PTH (pg/n		-65
Serum ph		-5.1
Serum cre		vomen, 0.4–1.1
Serum alb		-5.0
Total alka		115
BSAP (ng/ml)	72.6 ± 20.6 (7.1–588)	3.0–20.9
Serum NTx (nM BCE)	110.3 ± 26.7 (8–560)	5.4–24.2

Silverberg et al., JCEM 2009

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European Medical Agency (2008)

"for the reduction of hypercalcemia in patients with PHPT, for whom PTx would be indicated on the basis of serum calcium levels (as defined by relevant treatment guidelines), but in whom PTx is not clinically appropriate or is contraindicated "
http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000570/human_med_000903.jsp&mid=WC0p01ac058001d124.

U.S. Food and Drug Administration (2011)

"for the reduction of hypercalcemia in patients with parathyroid carcinoma and for the treatment of severe hypercalcemia in patients with PHPT who are unable to undergo parathyroidectomy"
http://www.fda.gov/Drugs/DrugSafety/ucm340551.htm.

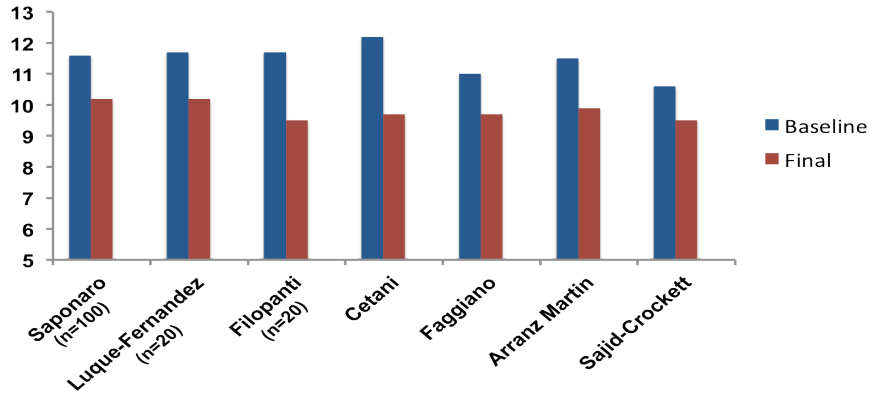
Approved only for adults

Trattamento non chirurgico

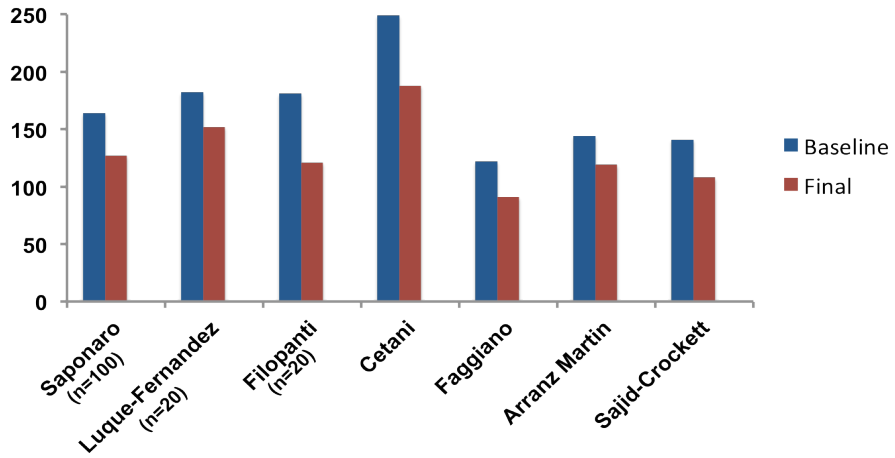
Cinacalcet

Patients with failed PTx, PTx contraindicated, inappropriate or refused
Mean baseline serum calcium 11.5 mg/dL
Median follow-up 9 months

Mean decrease 13.3%



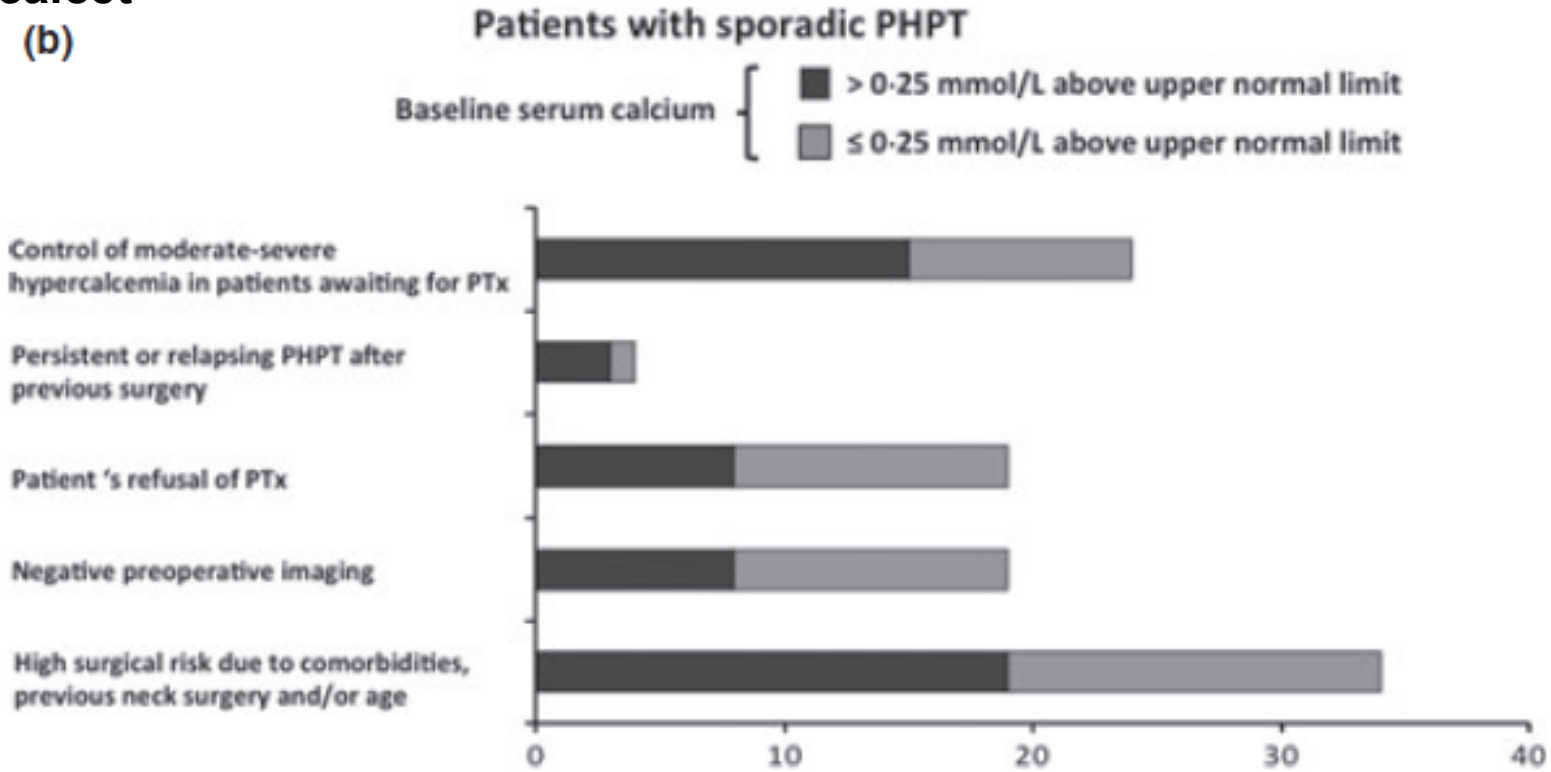
Mean decrease 22.6%



Trattamento non chirurgico

Cinacalcet

(b)



Saponaro et al., Clin Endocrinol 2013

Cinacalcet + bisphosphonates

Author	N.	Mean age (yr)	Therapy duration (months)	Serum calcium mg/dL		Plasma PTH (pg/mL)		BMD changes (%)	
				Baseline	Final	Baseline	Final	Spine	Hip
Faggiano	10	67	12	11.1±0.2	9.5±0.1	145±24	103±9	+9.6 ±1.4	+3.9 ±1.0
Keutgen	17	72	12	10.8±0.6	10.1±0.7	116±85	93±67	+25	-6
Cetani *	8	75	12	12.0±0.7	9.9±0.3	272±142	276±171	-	-

*** Patients were already given bisphosphonates when cinacalcet was started**

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Potential candidates:

- Metastatic parathyroid cancer
- Patients with contraindication to surgery
- Patients with complication of previous neck surgery
- Patients unwilling to undergo surgery
- Failed parathyroidectomy
- Selected asymptomatic patients who met surgical criteria for PTX

No single drug is effective in controlling clinical manifestations of PHPT

Targeted medical approach: Aims

- To improve bone mass: Antiresorptive therapy
- To decrease serum calcium: Cinacalcet
- To both aims: Combined antiresorptive therapy and cinacalcet

Trattamento non chirurgico

Thank you for your attention