Bari,
7-10 novembre 2013

L'OSTEOMALACIA

DALLA TEORIA ALLA PRATICA:

DISCUSSIONE INTERATTIVA

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CASO CLINICO

- **Età: 46 anni**
- **Sesso femminile**
- **Indice di Massa Corporea: 27.4 Kg/m^2**
- **Menarca a 11 anni.**
- **Cicli mestruali regolari per ritmo, frequenza e durata**
- **Scolarità: Diploma di scuola media superiore**
- **Matrimonio contratto a 27 anni con un non consanguineo coevo**
- **Due figli (1 maschio ed 1 femmina) in apparente buona salute**
- **Attività lavorativa: Casalinga**
- **Anamnesi familiare: positiva per nefrolitiasi recidivante. Negata familiarità per ipostaturismo e/o deformità ossee**

ANAMNESI PERSONALE REMOTA

- ✓ Comuni esantemi infantili guariti senza reliquati.
- ✓ Appendicectomia a 16 anni. Due tagli cesarei
- ✓ Nefrolitiasi da sali di ossalato di calcio a 30 anni.

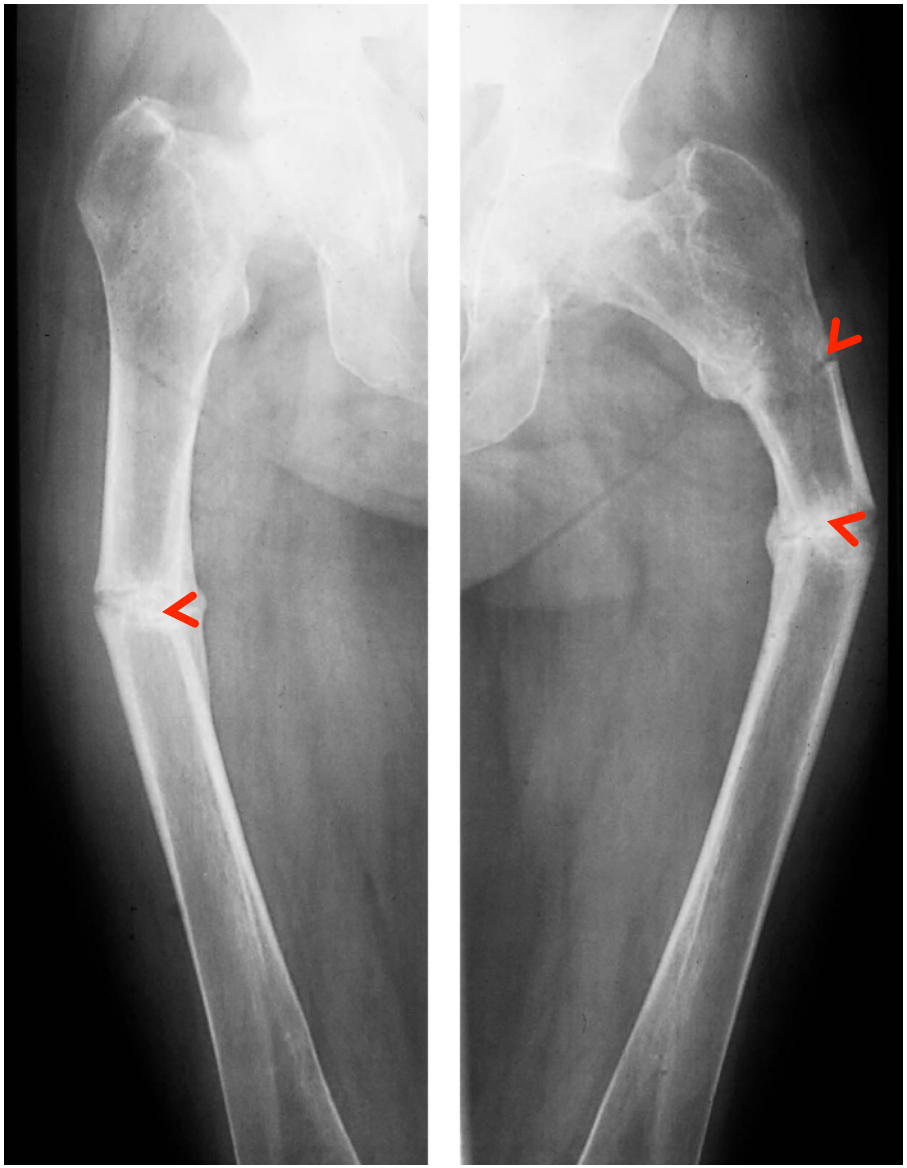
ANAMNESI FARMACOLOGICA

- ✓ Muta fino a 42 anni

ANAMNESI PERSONALE PROSSIMA

- ✓ Da circa quattro anni dolori ossei e muscolari diffusi, prevalentemente localizzati ai cingoli, associati a notevole impotenza funzionale.
- ✓ Frattura atipica di femore circa 24 mesi prima della visita medica in assenza trauma causale

- **Demineralizzazione diffusa**



- **Frattura a legno verde**
- **Coinvolgono una regione ossea ricca di osso trabecolare e sottoposta a carico meccanico**

- **Pain medical score [A]: 9 (range 0-9)**
- **Medical pain score [A]: 9 (range 0-9)**
- **Muscle weakness score [B]: 48 (range 0-60)**
- **EMG: non evidenti segni di danno neurogeno**

A) Tong D, Gillick L, Hendrickson FR (1982) The palliation of symptomatic osseous metastases: final results of the Study by the Radiation Therapy Oncology Group. Cancer 50: 893-899

B) Seibel M (1996) Neuromuscular examination. In: Valmassy RL (ed) Clinical Biomechanics of the Lower Extremities. 1st ed. Mosby, St. Louis, MO, USA, p 207–221

- **VES: 32 mm/1h**
- **PCR: 20 mg/l**
- **Quadro proteico elettroforetico come da flogosi**
- **Proteinuria di Bence-Jones negativa**
- **Emocromo: Anemia microcitica ipocromica; neutrofilia relativa**

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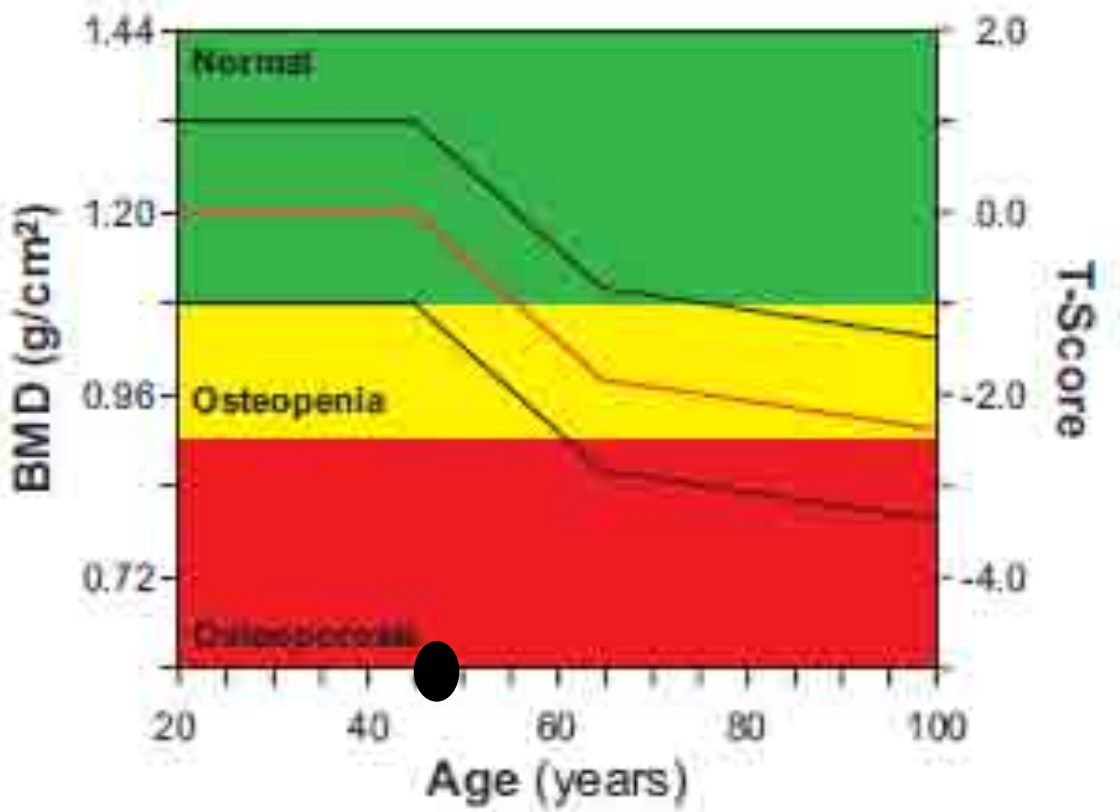
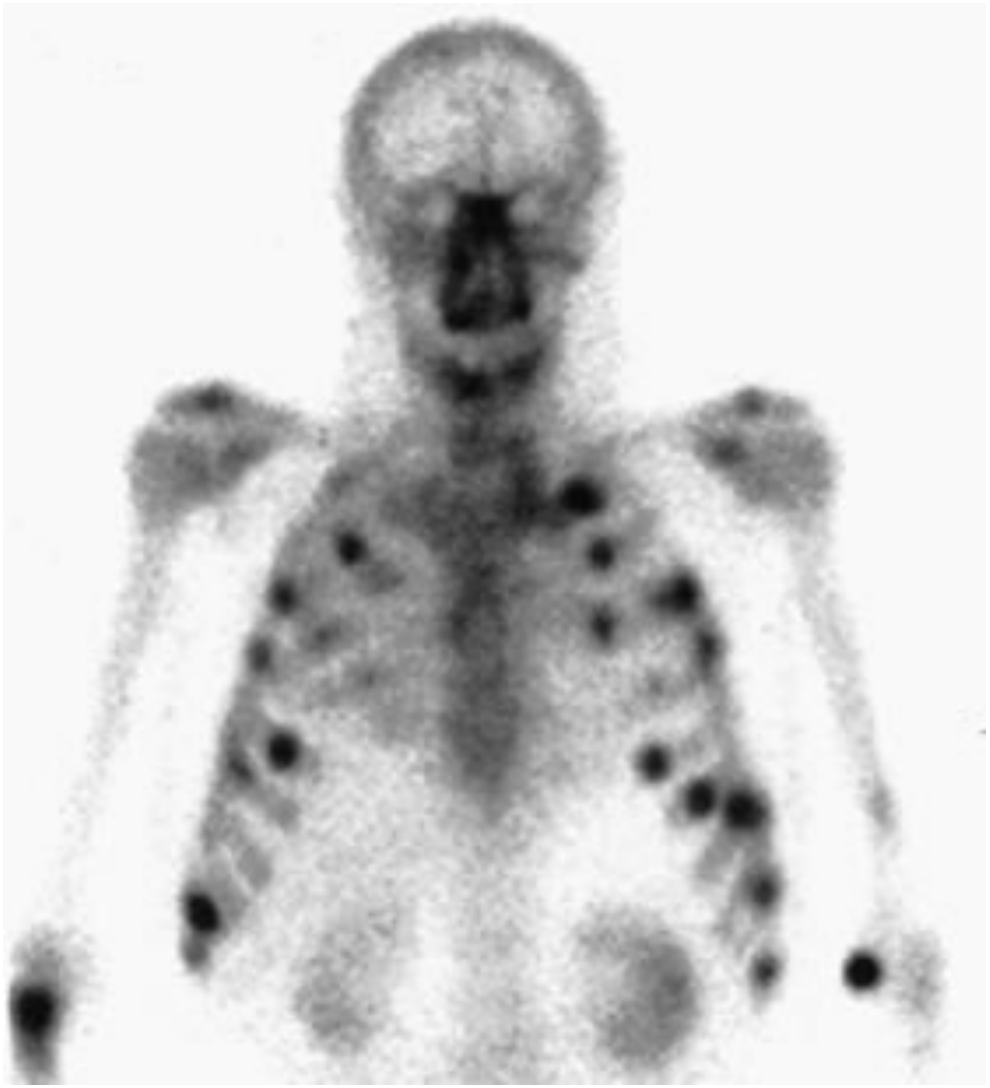
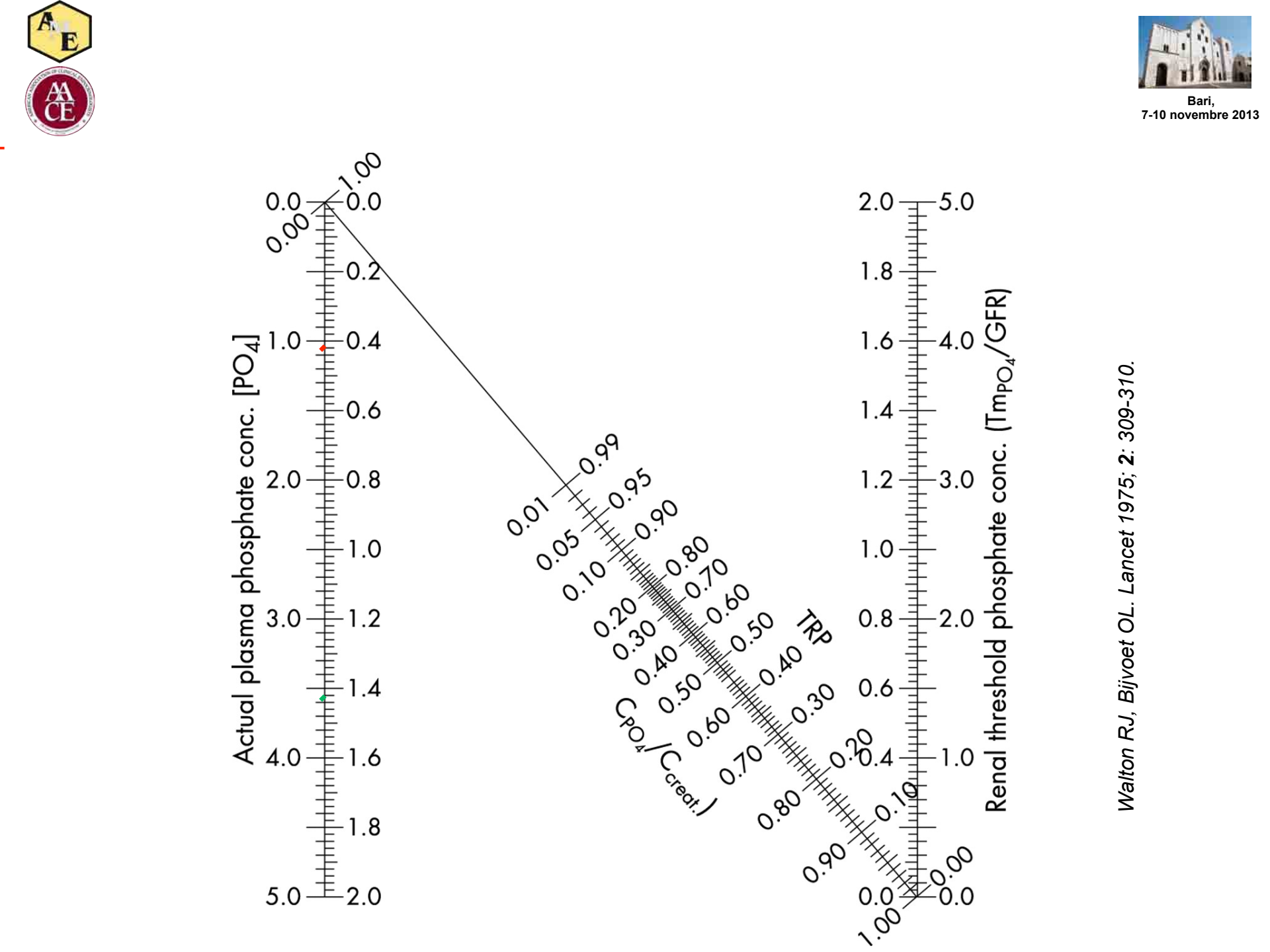
Parametro		V.N.
CALCEMIA TOTALE	2.37 mmol/L	2.37±0.11
CALCIO IONIZZATO	1.25 mmol/L	1.24±0.06
FOSFOREMIA	0.48 mmol/L	1.14±0.19
FOSFATASI ALCALINA TOTALE	269 U/l	98±15
MAGNESEMIA	0.95 mmol/L	1.01±09
$25OHD_3$	74,9 pmol/L	76.4±10
$1,25(OH)_2D_3$	78.4 pmol/L	87.2±20
PTH	2.57 pmol/L	2.49±0.57
CLEARANCE CREATININA	109 ml/min/1.73 m^2	107±15


1.44
1.20
0.96
0.72
Normal
Osteopenia
Osteoporosis
BMD (g/cm²)
2.0
0.0
-2.0
-4.0
T-Score
20
40
60
80
100
Age (years)





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Actual plasma phosphate conc. [PO_4]

0.0 0.00 1.00
1.0 0.2 0.8
2.0 0.4 0.6
3.0 0.6 0.4
4.0 0.8 0.2
5.0 1.0 0.0

$C_{PO_4}/C_{creat.}$

0.01 0.99
0.05 0.95
0.10 0.90
0.20 0.80
0.30 0.70
0.40 0.60
0.50 0.50
0.60 0.40
0.70 0.30
0.80 0.20
0.90 0.10
1.00 0.00

TRP

2.0 5.0
1.8 4.5
1.6 4.0
1.4 3.5
1.2 3.0
1.0 2.5
0.8 2.0
0.6 1.5
0.4 1.0
0.2 0.5
0.0 0.0

Renal threshold phosphate conc. (Tm_{PO_4}/GFR)

*Walton RJ, Bijvoet OL. Lancet 1975; **2**: 309-310.*

- **Fratture patologiche con astenia marcata e dolori muscolari**
- **sPO_4^{2-} & TmPi/GFR ridotti**
- **Calcemia nei limiti**
- **iPTH &1,25$(OH)_2D_3$ nei limiti**
- **BMD patologica**
- **Scintigrafia ossea con ipercaptazione simmetrica**

↓

DISORDINE DA PERDITA RENALE DI FOSFATI

(Prié D, et al. N Engl J Med. 2002;347(13):983-91)

↓

FGF-23

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Parametro	Valore	
CALCEMIA TOTALE	2.37 mmol/L	2.37±0.11
CALCIO IONIZZATO	1.25 mmol/L	1.24±0.06
FOSFOREMIA	0.48 mmol/L	1.14±0.19
FOSFATASI ALCALINA TOTALE	269 U/l	98±15
MAGNESEMIA	0.95 mmol/L	1.01±09
$25OHD_3$	74,9 pmol/L	76.4±10
$1,25(OH)_2D_3$	78.4 pmol/L	87.2±20
PTH	2.57 pmol/L	2.49±0.57
CLEARANCE CREATININA	109 ml/min/1.73 m^2	107±15
FGF-23 C-term	1158 UR/ml	27±11

Biological Variability of Plasma Intact and C-Terminal FGF23 Measurements

Edward R. Smith, Michael M. Cai, Lawrence P. McMahon, and Stephen G. Holt

J Clin Endocrinol Metab, September 2012, 97(9):3357–3365

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Tumor-Induced Osteomalacia

American Society for Bone and Mineral Research

DIFFERENTIAL DIAGNOSIS

However, TIO is biochemically indistinguishable from several inherited forms of hypophosphatemic rickets: X linked hypophosphatemic rickets (XLH) and autosomal dominant hypophosphatemic rickets (ADHR).[11] Because patients with XLH and ADHR exhibit a variable age of onset, it is critical to take a careful family history in patients with hypophosphatemia. The clinical consequences of TIO are typically present for many years before the causal tumor is identified; this further obscures the clinical distinction between TIO and inherited forms of hypophosphatemic, vitamin D–resistant rickets. In contrast to XLH, patients with TIO exhibit symptoms of weakness, pain, and fractures that are more severe and disabling. Stress and insufficiency fractures are more typical of TIO, whereas lower extremity deformity and short stature are characteristic of XLH and ADHR. Serum FGF-23 levels are generally elevated in patients with TIO but are also elevated in patients with ADHR and some patients with XLH. Furthermore, normal serum FGF-23 levels do not eliminate the diagnosis of TIO.[11,12] The diagnosis of TIO is dependent on the identification of the culprit tumor and remission of the syndrome after complete tumor resection. Genetic testing of the *PHEX* and *FGF-23* genes, which are defective in XLH and ADHR, respectively, is commercially available and may be indicated when a definitive diagnosis is necessary.[13]

Clinica

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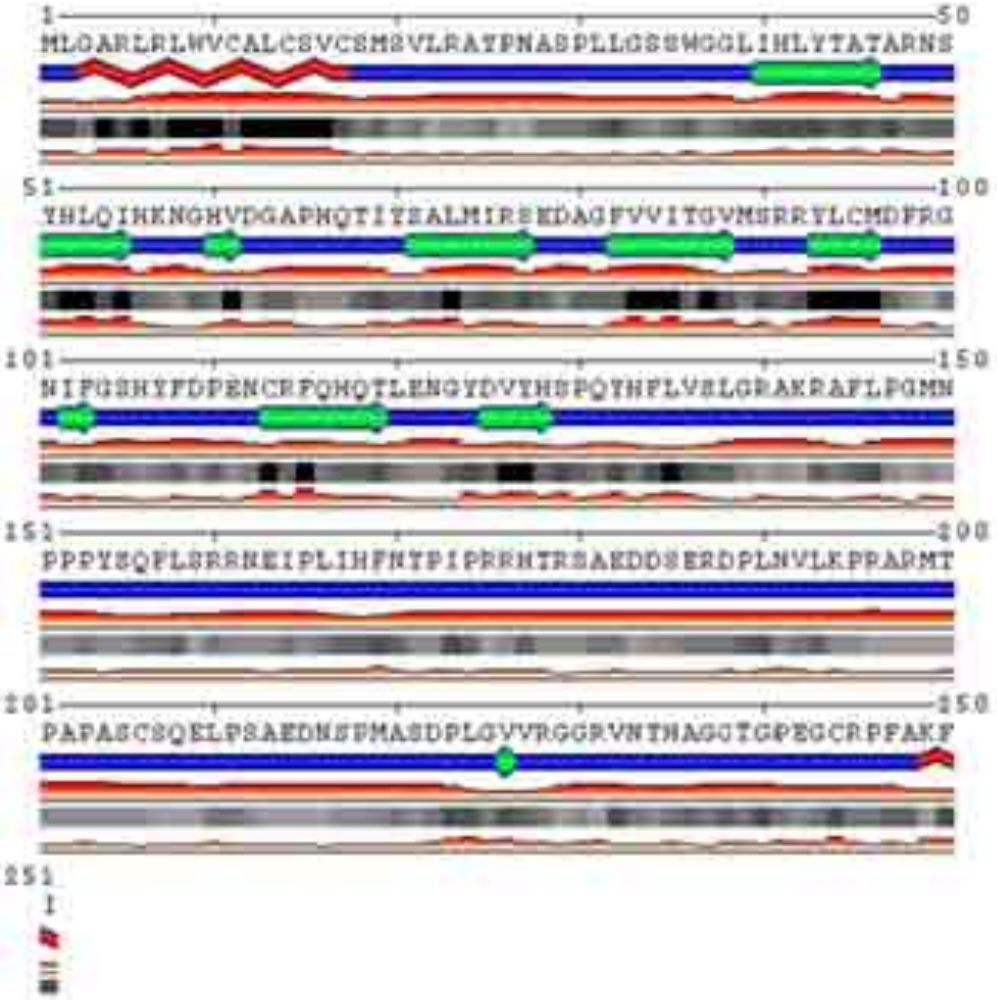

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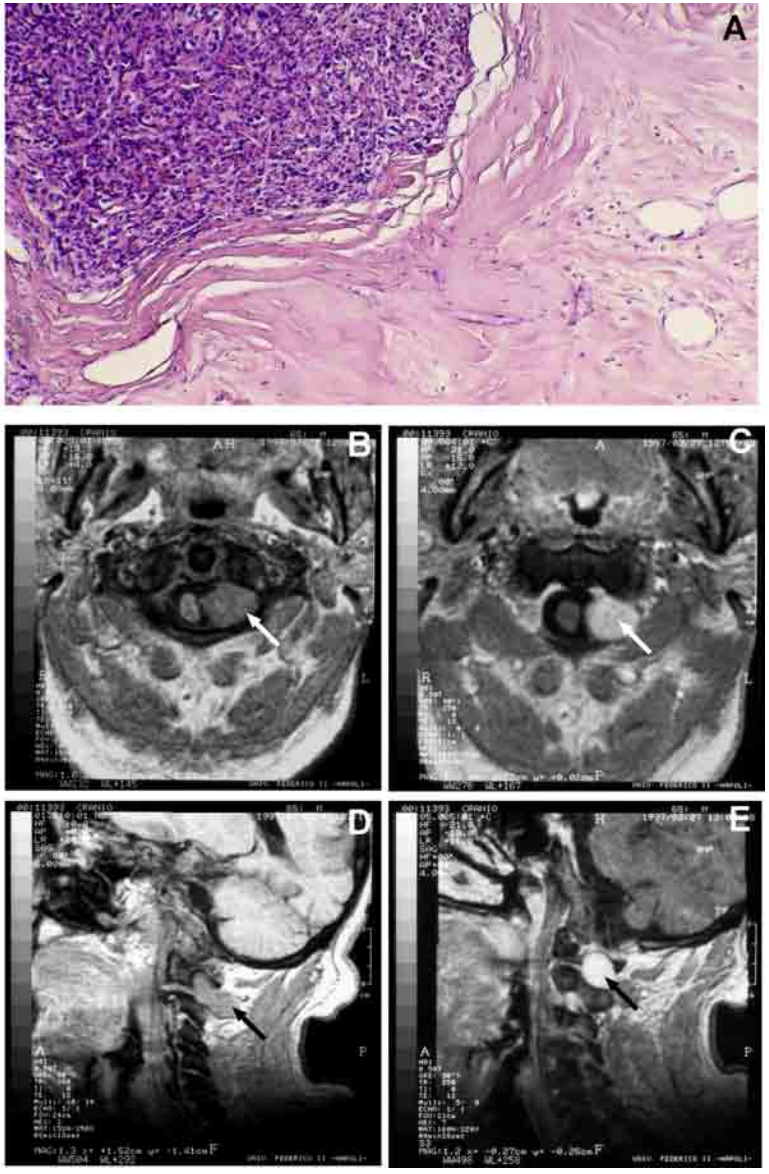

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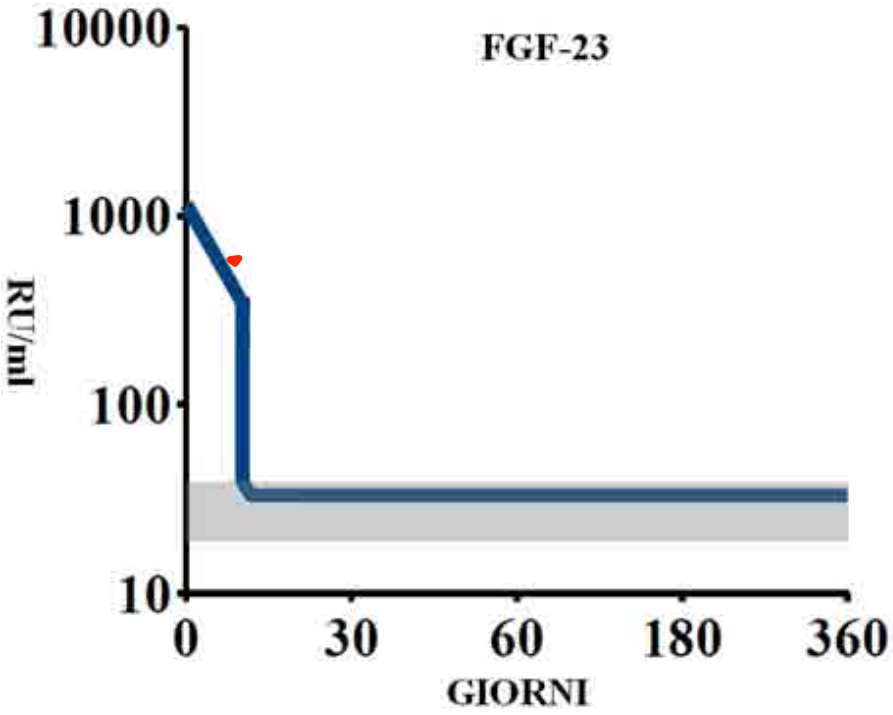
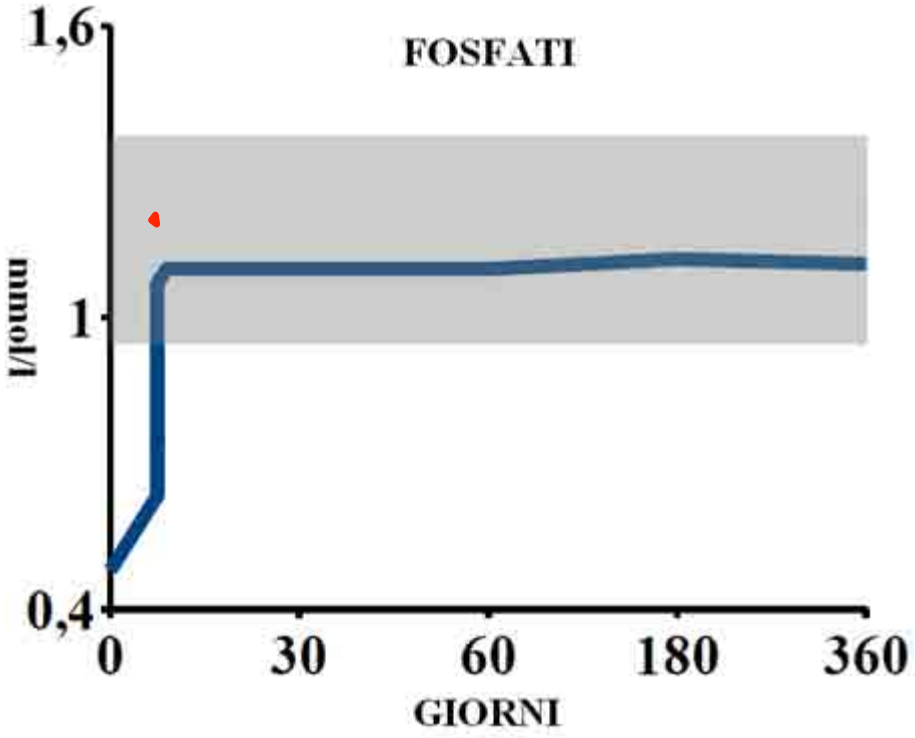
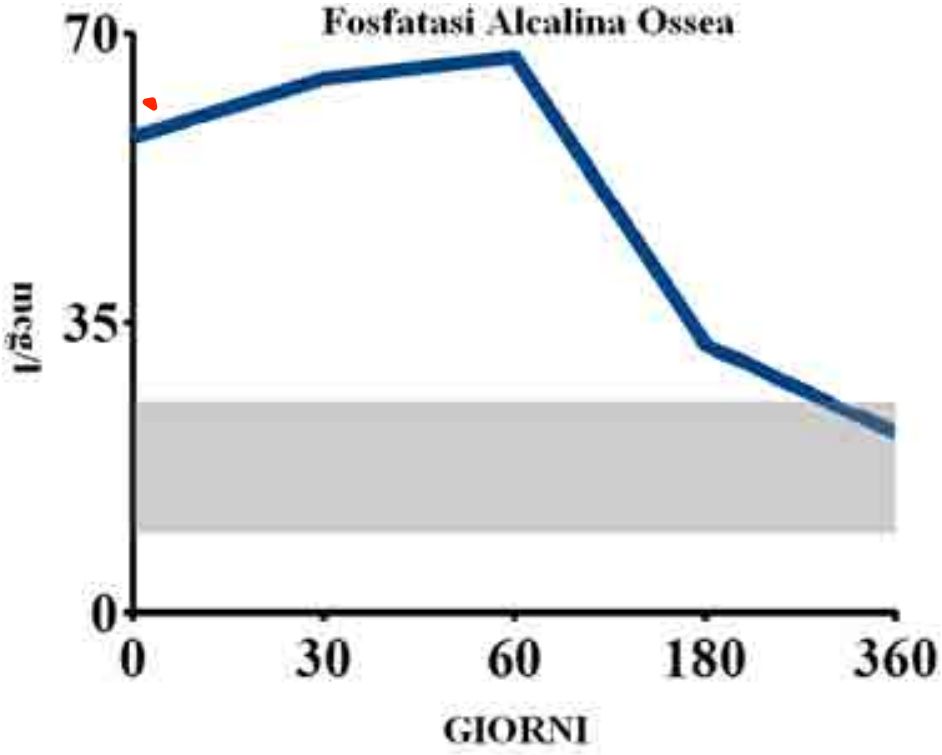
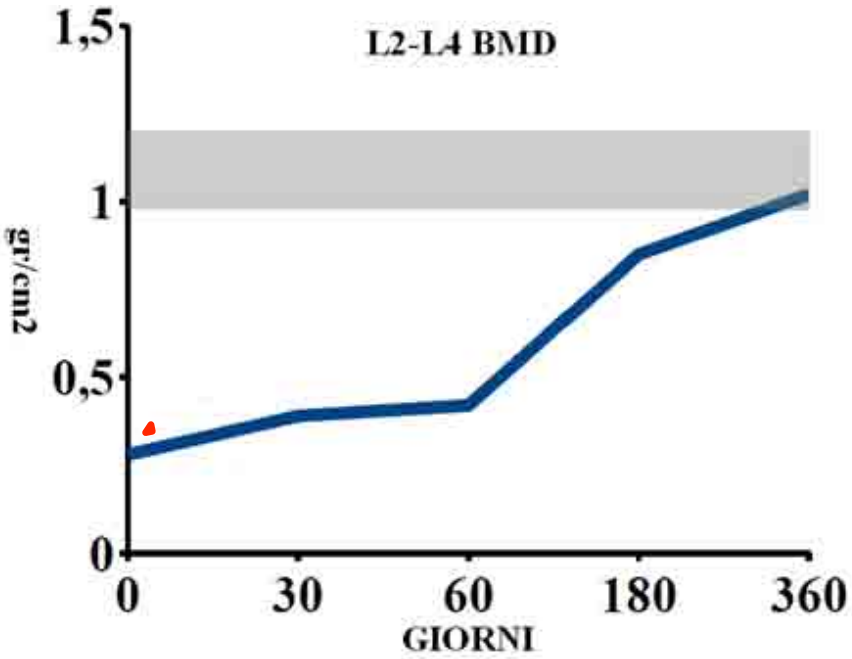


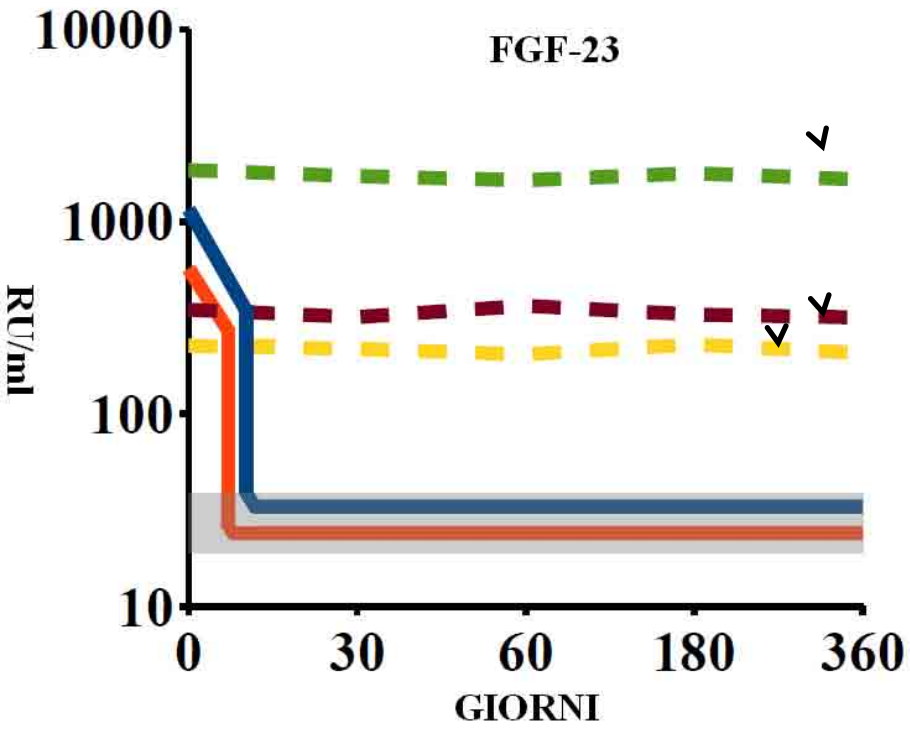


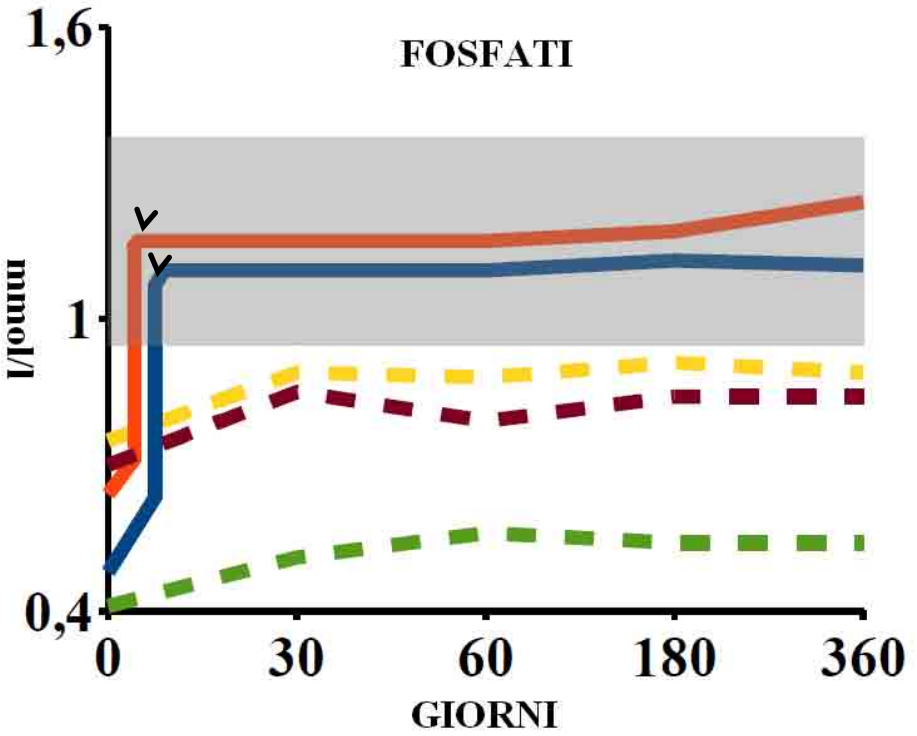

Fosfatasi Alcalina Ossea
70
35
0
mcg/l
0
30
60
180
360
GIORNI

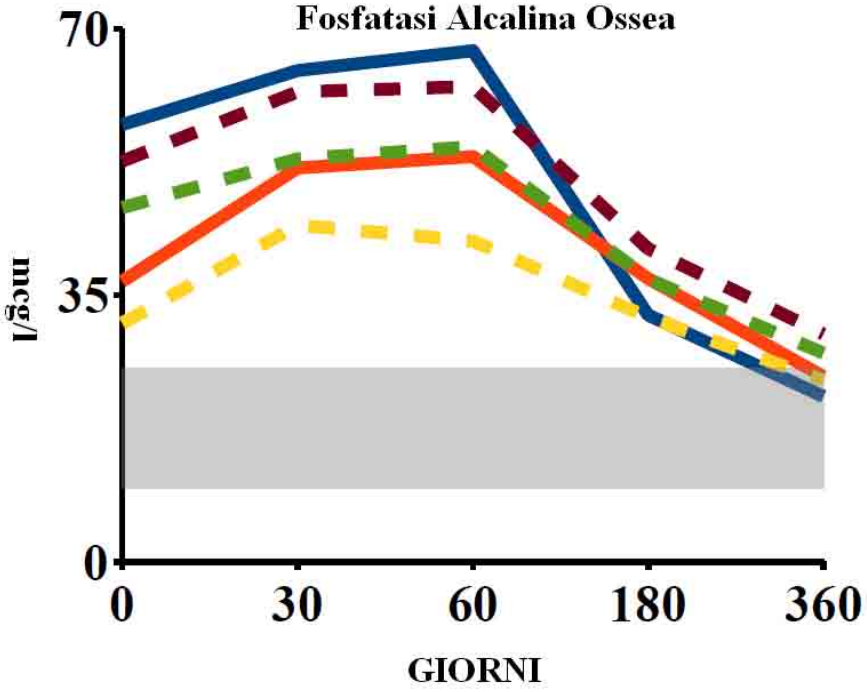

L2-L4 BMD
1,5
1
0,5
0
gr/cm2
0
30
60
180
360
GIORNI

- CALCITRIOLO (1-3 µg/die)
  FOSFORO (2g/die)

- EXERESI CHIRURGICA



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mcg/l
0
30
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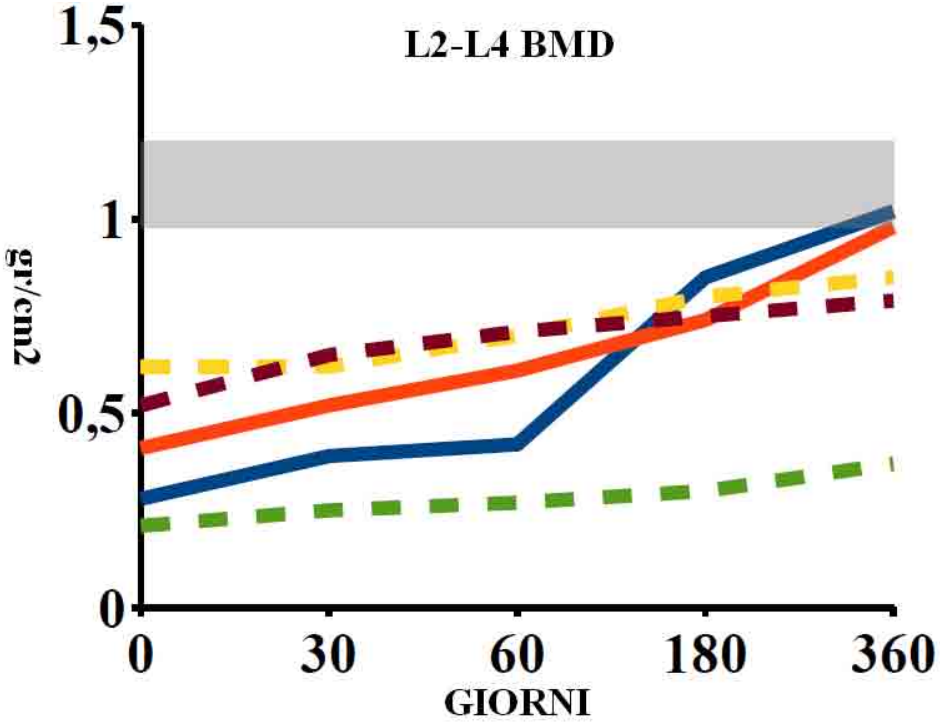
GIORNI


L2-L4 BMD
1,5
1
0,5
0
gr/cm2
0
30
60
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360
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