Bari,
7-10 novembre 2013

HOT TOPICS IN OSTEOPOROSIS
From theory to pratice

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Case Study:Anna

53-year-old post-menopausal woman

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Presents for examination for recent fragility fracture.

✓MRI: old vertebral fractures (D11,L1, L2,L3 – history of trauma in 2010 with normal BMD) + recent vertebral fracture (D12).

e L1-L4 score/Z-score)	DXA – femoral neck (BMD/T-score/Z-score)
	0981/-1
/-0,7	0,933/-1,3/-0,4

rule out other causes of secondary osteoporosis

sphocalcic metabolism

Case Study:Anna

53-year-old post-menopausal woman

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- Family history: father, hip fragility fracture at age 50
- Menarche at age 12, regular menses, menopause at age 45, no HRT; non smokers, no alcohol, adequate calcium intake, no regular exercises
- Past medical history: trauma in 2010 →vertebral fractures. No history of systemic glucocorticoids.
- Physical examination: 60 Kg x160 cm, BMI:23,4 Kg/m2 , accentuation of the dorsal kyphosis, low back pain, no sign of Cushing ‘s disease
- On no medications

Case Study:Anna

53-year-old post-menopausal woman

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- ✓ ? Laboratory tests to rule out other causes of secondary osteoporosis
- ✓ ? Assessment of phosphocalcic metabolism

FRAX and DXA are not useful to decide about the therapy
→ fragility vertebral fracture places Anna at high risk category

GUIDELINES

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- ✓ *National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. http://www.nof.org/files/nof/public/content/file/344/upload/159.pdf. Accessed January 3, 2013.*

- ✓ *European guidance for the diagnosis and management of osteoporosis in postmenopausal women.Kanis JA et al; Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) and the Committee of Scientific Advisors of the International Osteoporosis Foundation (IOF).Osteoporos Int. 2013 Jan;24(1):23-57.*

FOLLOW UP IN GUIDELINES

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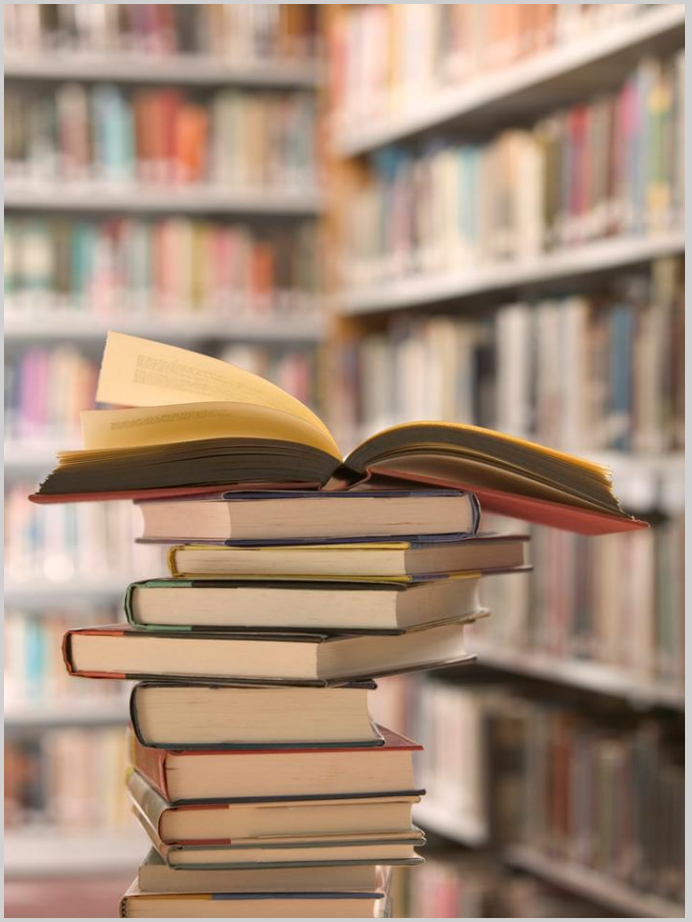
- Patients are tipically monitoring using:

- ❑ BMD
- ❑ (BMTs)
- ❑ new low trauma fractures

- Biphosphonate “Drug holiday” after 3-5 y



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Current clinical practice guideline do not provide target to determine if treatment has been effective

→ satisfactory reduction in fracture risk

Treat-to-target

J Clin Endocrinol Metab. 2013 Mar;98(3):946-53. Treat-to-target for osteoporosis: is now the time?

Lewiecki EM, et al

BMD AND FRACTURES RISK

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BMD increase is usually seen as an indication of therapeutic success

Limits:

- ✓ Disagreement on that relationship:
  - in some analyses: reduction in fracture risk with bisphosphonate therapy with no change or a loss in BMD (1, 2)
  - with zoledronic acid (3) and denosumab (4), a strong correlation between BMD increase and fracture risk reduction.
- ✓ LSC
- ✓ Only examinations carried out in the same center are comparable
- ✓ Validated centeres are required
- ✓ Structural abnormalities, that may increase BMD, particularly in spine, without imparting an increase in bone strength.

1) Bauer DC et al. J Bone Miner Res. 2004;19(8):1250–1258.
2) Watts NB, et J Bone Miner Res. 2005;20(12):2097–2104.
3) Jacques RM, et al. J Bone Miner Res. 2012;27(8):1627–1634.
4) Austin M, et al. J Bone Miner Res. 2012;27(3):687–693.

BMTs

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- with anabolic therapies (1-3 month)
- with antiresorptive therapies (3-6 month)

Limits:

- ✓ Lack of clarity in optimal choice of BTM
- ✓ Assay variability
- ✓ Reproducibility of the examination
- ✓ Need to consider the LSC of specific biochemical marker ("precision error"x 2,77)
- ✓ Validate center are required
- ✓ Problematic availability and affordabilty in some world regions

HIP T-score AND "DRUG HOLIDAY"

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Evidence supporting the utility of T-scores at the hip to decide about "drug holiday"

-Continuing alendronate for 10 years instead of stopping after 5 years → reduction in the risk of nonvertebral fractures for women without prevalent vertebral fractures whose femoral neck T-scores were −2.5 or less after 5 years of therapy; not reduced in with femoral neck T-scores >−2.0 after 5 years of therapy (1-2).
-A femoral neck or total hip T-score <−2.5 after 3 annual doses of zoledronic acid was predictive of increased risk of new morphometric and nonvertebral fractures in women subsequently randomized to stop treatment (3),

Limits:

✓No informations about patientes with prevalent vertebral fracture.

1) Schwartz AV, et al. J Bone Miner Res. 2010;25(5):976–982.
2) Black DM, et al. JAMA. 2006;296(24):2927–2938.
3) Cosman F et al. J Bone Miner Res. 2011;26(Suppl 1):S79.

To optimize the follow up it's necessary...

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- Having in mind the limitations of the assessment tools available
- Make appropriate corrections if is necessary
- Instruct the patient to get the most reliable data
- Continuous up to date

Case Study:Francesca

54-year-old post-menopausal woman

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First examination for osteoporosis (6/2012)

Past medical hystory: breast cancer at age 52

Hstologically: Infiltrating ductal breast cancer pT2 pN1a,G3; ER-, PgR-, HER 2-, K67 90% -- surgery (quadranctectomy with axillary dissection) CEF chemoterapy (cyclophosphamide/ epirubicin/fluorouracil). Bone scintigraphy 2010-2012: negative.

No AIs/Tamoxifen

	DXA spine L1-L4 (BMD/T-score/Z-score)	DXA femo (BMD/T-s
10/2010	0,778/-2,7/-1,9	----------
1/2012	0,782/-2,7/-1,7	----------

- ✓ No recent assessment of phosfocalcic metabolis
- ✓ No laboratory test to rule out other causes of se

Case Study:Francesca

54-year-old post-menopausal woman

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- Family history: none significant
- menarche at age 9, regular menses, menopause at age 47, no HRT; stop smoking at age 26; no alcohol; adequate calcium intake; physically active.
- Physical esamination: 66 Kg x163 cm, BMI: 24,9 Kg/m2
  mild accentuation of dorsal kyphosis, no back pain, no signs/simptoms of neuropaty
- No comorbidity. No history of long-term systemic corticosteroids use
- **On therapy: calcium/vitD3 600+400/daily; Alendronate 70 mg/w (from 1/13)**

Case Study:Francesca

54-year-old post-menopausal woman

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Bloodwork :

- ✓ for assessment of phosfocalcic metabolism → normal calcium, phosphate and PTH level; vitamin 25-OH-D deficency: 16 ng/ml; normal values of OC, ALP, cross links.
- ✓ to rule out other causes of secondary osteoporosis → normal levels of TSH, celiac disease antibody panel, QPE, complete blood count, creatinine

Lateral thoraco-lumbar spine X-ray is ordered to rule out vertebral fractures (mild dorsal kyfosis) : negative

Case Study:Francesca

54-year-old post-menopausal woman

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Cancer without known skeletal metastases and not requiring therapy to lower sex steroid

Risk assessment and therapy should be applied as in non-cancer patients

Rizzoli R, et al; for the International Osteoporosis Foundation Committee of Scientific Advisors Working Group on Cancer-Induced Bone Disease. Osteoporos Int. 2013 Oct 22.

Case Study:Francesca

54-year-old post-menopausal woman

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Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: Italy Name/ID: F.R. About the risk factors

Questionnaire:

1. Age (between 40 and 90 years) or Date of Birth
   Age: 54 Date of Birth: Y: M: D:
2. Sex — Male / Female
3. Weight (kg): 66
4. Height (cm): 163
5. Previous Fracture — No / Yes
6. Parent Fractured Hip — No / Yes
7. Current Smoking — No / Yes
8. Glucocorticoids — No / Yes
9. Rheumatoid arthritis — No / Yes
10. Secondary osteoporosis — No / Yes
11. Alcohol 3 or more units/day — No / Yes
12. Femoral neck BMD (g/cm^2)

Select BMD

Clear Calculate

BMI: 24.8

The ten year probability of fracture (%)

without BMD

Major osteoporotic	3.1
Hip Fracture	0.3

Print tool and information

Risk factors

Weight Conversion

Pounds → kg Convert

Height Conversion

Inches → cm Convert

00137443

Individuals with fracture risk assessed since 1st June 201

Traduzione italiana approvata SIMG (Società Italiana di Med

Case Study:Francesca

54-year-old post-menopausal woman

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✓Frax index → low risk→ no therapy

✓Guidelines→ therapy (after appropriate evaluation)

✓Nota 79 doesn' t repay that therapy

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Questions…

- **Why** to treat?
- How long to treat?

Case Study:Francesca

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52-year-old postmenopausal woman

- Family history: none significant
- menarche at age 9, regular menses, menopause at age 47, no HRT; stop smoking at age 26; no alcohol; adequate calcium intake; physically active.
- Past medical hystory: quadranctectomy supero-esterna destra 9/2010 (età: 52 anni)

Hstologically: Infiltrating ductal breast cancer pT2 pN1a,G3; **ER-**, PgR-, HER 2-, K67 90% --

If the BC was ER+? We are in 2010...

- Physical esamination: 66 Kg x163 cm, BMI: 24,9 Kg/m2, mild accentuation of dorsal kyphosis, no back pain, no signs/simptoms of neuropaty
- No comorbidity
- No history of long-term systemic corticosteroids use
- Vitamin 25-OH-D deficency
- T-score of spine L1-L4 -2,7 in 2010
- Lateral thoraco-lumbar spine X-ray: negative

SECONDARY OSTEOPOROSIS

AACE Postmenopausal osteoporosis guidelines, Endocr Pract 2010;16 (suppl 3)

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Table 9
Some Causes of Secondary Osteoporosis in Adults[a]

Endocrine or metabolic causes	Nutritional/ gastrointestinal conditions	Drugs	Disorders of collagen metabolism	Other
Acromegaly	Alcoholism	Antiepileptics[b]	Ehlers-Danlos syndrome	AIDS/HIV
Diabetes mellitus	Anorexia nervosa	Aromatase inhibitors	Homocystinuria due to	Ankylosing spondylitis
Type 1	Calcium deficiency	Chemotherapy/	cystathionine deficiency	Chronic obstructive
Type 2	Chronic liver disease	immunosuppressants	Marfan syndrome	pulmonary disease
Growth hormone deficiency	Malabsorption syndromes/	Depo-Provera	Osteogenesis imperfecta	Gaucher disease
Hypercortisolism	malnutrition (including	Glucocorticoids		Hemophilia
Hyperparathyroidism	celiac disease, Crohn	Gonadotropin-releasing		Hypercalciuria
Hyperthyroidism	disease, and gastric	hormone agonists		Immobilization
Hypogonadism	resection or bypass)	Heparin		Major depression
Hypophosphatasia	Total parenteral nutrition	Lithium		Myeloma and some
Porphyria	Vitamin D deficiency	Proton pump inhibitors		cancers
Pregnancy		Selective serotonin		Organ transplantation
		reuptake inhibitors		Renal insufficiency/
		Thiazolidinediones		failure
		Thyroid hormone (in		Renal tubular acidosis
		supraphysiologic		Rheumatoid arthritis
		doses)		Systemic mastocytosis
		Warfarin		Thalassemia

[a] AIDS = acquired immunodeficiency syndrome; HIV = human immunodeficiency virus.
[b] Phenobarbital, phenytoin, primidone, valproate, and carbamazepine have been associated with low bone mass.

BREAST CANCER AND FRACTURES

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<u>Women who have been treated medically for breast cancer may be at increased risk for bone loss and fractures :</u>

- ✓ The annual incidence of vertebral fractures is fivefold increase. Fivefold higher prevalence of vertebral fractures in women with breast cancer, but without bone metastases, than in women of the same age [1].
- ✓ fracture rates in breast cancer is a 15 % increase, after adjustment for age, ethnicity, weight and geographic location [2].

1)Kanis JA,et al(1999) Br J Cancer 79:1179–1181
2)Chen Z, et al (2005) Arch Intern Med 165:552–558

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BONE AND BREAST CANCER TREATMENT

Premenopausal women

- CHT-induced hypogonadism
  BL 8%s,4%h 1°y (NR), RF+++
- GnRH agonists
  BL 6%/anno (R), RF-
- AIs
  RF e BL+++ (NR)
- Tamoxifene
  BL + (R)

Postmenopausal women

- CHT

//

- AIs
  FR e BL+++ (NR)
- Tamoxifene
  BL -

BL=BMD loss; RF: risk fractures; R= recovery; NR no recovery

Rizzoli R, et al; for the International Osteoporosis Foundation Committee of Scientific Advisors Working Group on Cancer-Induced Bone Disease. Osteoporos Int. 2013 Oct 22.

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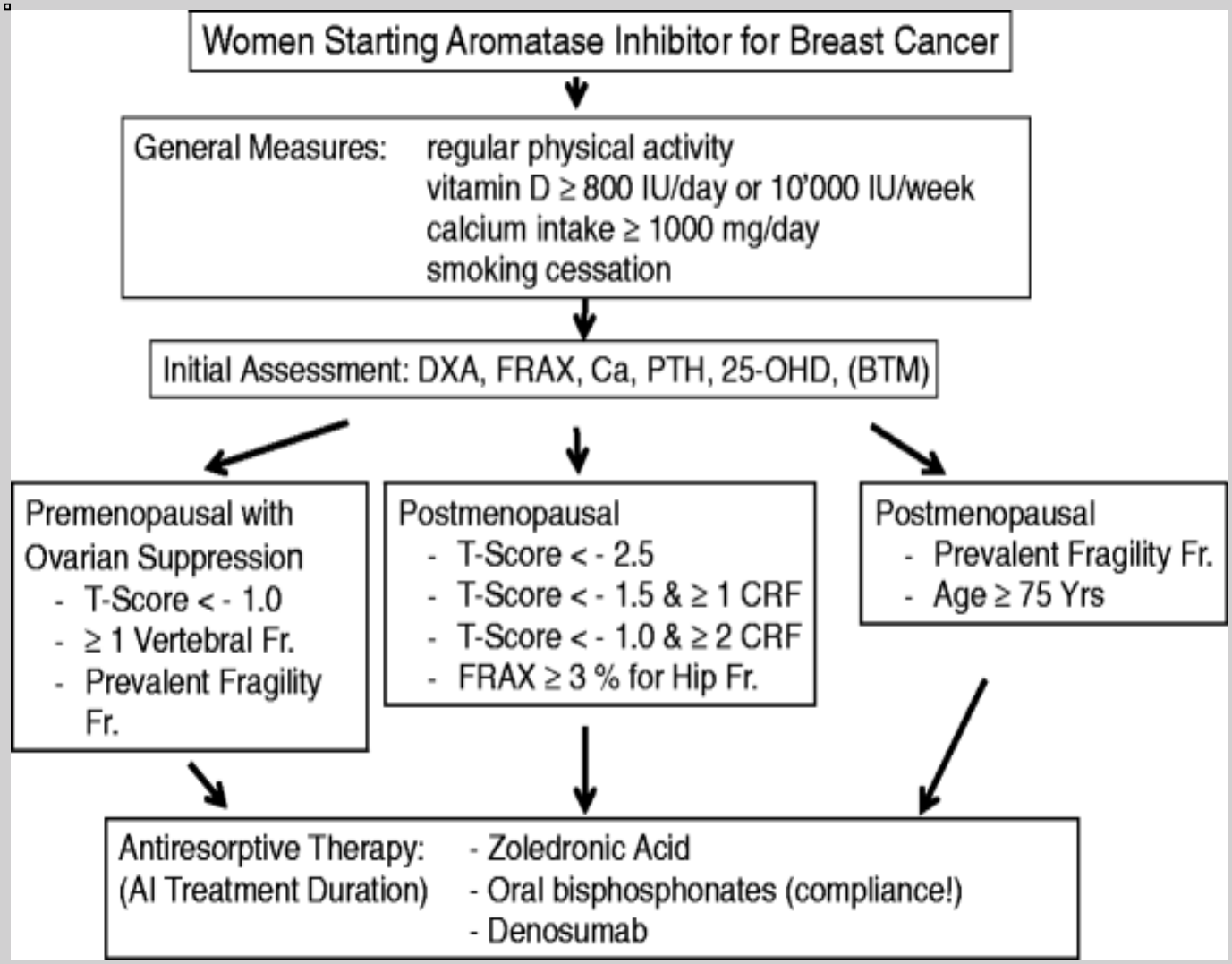

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Case Study:Francesca

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- No comorbidity

AIs → treatment for osteoporosis

- T-score of spine L1-L4 -2,7 in 2010
- Lateral thoraco-lumbar spine X-ray: negative

...in treatment of secondary osteoporosis keep in mind

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- Any secondary osteoporosis have peculiar aspects
- It could be necessary prevent bone loss to prevent fractures instead of only prevent it in osteoporotic patients
- Continuous up to date

Thanks for your attention!

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