Osteoporosis: Latest in Treatment Recommendations
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Disclosures
► Speaker Bureau:
  • Pfizer, Sanofi-Pasteur, Merck
  • Arbor, Pfizer, Sanofi, Merck

Objectives
Upon completion of this discussion, the participant will be able to
1. Discuss the pathophysiology of osteoporosis
2. Identify the non-pharmacologic and pharmacologic agents available for the treatment of osteopenia and osteoporosis
3. Compare and contrast newer pharmacologic agents with older agents with regard to benefits, risks, side effects, and drug interactions
Case Study

Anna: 57-year-old female

- Family History
  - Mother with hip fracture at age 75
  - Sister with vertebral fractures age 58
- PMH
  - No personal history of fractures (fragility or traumatic)
  - Hypothyroid with replacement (TSH - 0.89)
  - Asthma – present since childhood
  - TAH/BSO at age 40
  - Hypertension – diagnosed at age 46

Anna (continued)

- Social History
  - 2 oz white wine daily for past 10 years
  - Smoker – 15 pack year history of smoking
    - Discontinued 10 yrs ago; no relapses
  - Exercise:
    - Walks 1 mile daily - 20 minutes approximately 4 times per week
- Medications
  - Levothyroxine 125 mcg one daily for 20 years
  - HCTZ 12.5 mg one daily
  - Fluticasone/salmeterol 250/50 mcg 1 puff twice daily
  - Prednisone 1 – 2 x yearly
Anna (continued)

- Physical Examination
  - 65 inches
  - 111 pounds
- Labs
  - Vitamin D Level: 20.5 ng/mL
  - Serum Calcium: 8.9 mg/dL
- DXA Scan
  - Hip: T Score = -1.7
  - L-S spine: T Score = -2.0

1. What are her risk factors?
2. Is she at an increased risk for fracture?

Definition of Osteoporosis

Osteoporosis is defined as a skeletal disorder characterized by compromised bone strength predisposing a person to increased risk of fracture

Osteoporosis: Is There a Problem?

- Over 44 million Americans have or are at risk of osteoporosis.
  - 10 million people have osteoporosis
  - 34 million more are estimated to have low bone mass, which puts them at increased risk of developing osteoporosis and related fractures
- 80% of those affected are women; 20% are men.
- The prevalence of osteoporosis is expected to continue to increase with the growth of the elderly population.


Osteoporotic Fractures

An estimated 1 in 2 women over the age of 50 years will experience an osteoporosis related fracture.


Osteoporosis in Men

- Approximately, 20% of individuals with osteoporosis are men.
- 8 – 10 million men have osteopenia or osteoporosis.
- ~13% lifetime risk of sustaining a fracture of the hip, spine, or distal forearm (compared to 40% in women).
- Mortality is significantly higher in men than in women following fracture of the hip or spine.

Hip Fractures in Men Can Lead to Disability and Death

- Men are twice more likely to die within 1 year of a hip fracture than are women.\(^2\)
- Osteoporotic fractures are associated with a 3.2 fold increase in mortality in men.\(^3\)


Why is Osteoporosis Such a Widespread Problem?

- Lack of education and awareness
- Sedentary lifestyles
- Calcium and Vitamin D intake
- Alcohol intake
- Cigarette smoking
- *Carbonated drinks
- Aging population
- Certain medications
- Underdiagnosis and undertreatment
- Poor medication adherence

   Rockville MD: US Department of Health and Human Services, Office of the Surgeon General; 2004

Underdiagnosed / Undertreated?

- Many patients are undiagnosed because this is often a silent disease until a fracture occurs.
  - Emphasis must be on early diagnosis and treatment, regardless of symptoms.
- Adherence to chronic medications is poor
  - Many new treatment options are now available
    - Routes of delivery: Oral, Injection, IV, subcutaneous administration
    - Frequency options: Daily, weekly, monthly, quarterly, annually

   Rockville MD: US Department of Health and Human Services, Office of the Surgeon General; 2004
Incidence of Fracture Among Women

![Graph showing incidence of fractures among women]  

Incidence of Fractures: Vertebral vs. Hip

- Vertebral Fractures – 700,000 annually
- Hip Fractures – 300,000 annually


Osteoporotic Fractures

- Although much of the discussion in the literature speaks to hip fractures and the increased risk of morbidity and mortality, there are important additional messages:
  - Hip fracture rates begin to increase significantly at the age of 70 and are associated with significant morbidity and mortality
  - Vertebral fractures, often silent, are also associated with significant morbidity and mortality yet tend to occur in the younger individual: 55 +

Health Impact of Vertebral Fractures

- Vertebral fracture is often unrecognized
- Patients who have a vertebral fracture
  - Are at greater risk of any subsequent fracture
  - May become unable to walk unassisted
  - Lose height
  - May experience pain
  - Are at greater risk of death


Pathophysiology of Osteoporosis

Bone Remodeling

- Resting Phase
- Activation
- Resorption
- Reversal
- Formation
Bone Growth and Density

- Childhood: bones grow in length and density
- Teen years: maximum height is reached, but bones continue to become more dense
- Peak bone mass or density: achieved at age 30
- After age 30: Bones slowly start to lose density or strength


Pathophysiology of Osteoporosis

- Bone remodeling occurs throughout an individual’s lifetime
  - In adults, osteoclasts (bone resorption) is balanced by that of osteoblasts (bone formation)
- Diminishing estrogen levels with menopause lead to excessive bone resorption
  - Postmenopausal women lose 12% of bone mass over 6 years, beginning 2 years before the last menses; followed by 1 – 2% loss per year thereafter.


Contrast of Healthy and Osteoporotic Bone

Healthy Bone

Osteoporotic Bone

Images by David W. Dempster, PhD, 2005
### Assessment of the Individual At Risk For Osteoporosis

- **Clinical History**
  - Risk factors
  - Physical symptoms
  - Perceived loss of height
- **Physical Examination**
- **Bone Densitometry**
- **Bone Turnover Markers**
  - N-telopeptide (NTX – bone formation) and C-telopeptide (CTX – bone resorption)
- **Additional Testing**
  - 25-hydroxyvitamin D levels: 25(OH)D

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### Osteoporosis Risk Factors

- Advanced age
- Personal history of fracture after age 50
- History of a fracture in a primary relative
- BMI < 19
- Current low bone mass
- Female
- Family history of osteoporosis
- Estrogen deficiency
- Amenorrhea
- Anorexia
- Low lifetime calcium intake
- Vitamin D deficiency
- Use of certain medications
  - Oral corticosteroids
  - Anticonvulsants
- Presence of certain chronic medical conditions
- Low testosterone levels in men
- An inactive lifestyle
- Cigarette smoking
- Excessive use of alcohol
- Being Caucasian or Asian

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Contributing Factors To Low Bone Mass

Lifestyle factors
- smoking
- excessive alcohol
- immobilization

Endocrinopathies
- hyperparathyroidism
- cortisol excess
- hyperthyroidism
- hypogonadism

Medications
- glucocorticoids
- immunosuppressives
- anticonvulsants
- suppressive doses of T4
- GnRH agonists

Abnormal Calcium Balance
- low calcium intake
- GI malabsorption
- renal calcium wasting

Other Medical Problems
- myeloma
- chronic renal disease
- chronic liver disease

Adapted from American Association of Clinical Endocrinologists, www.AACE.com; accessed 01-12-08

Vitamin D Deficiency

- 50% of women with an osteoporotic hip fracture¹
  - Severely deficient (≤12 ng/ml)
- 51% of healthy black adolescents in Boston²
- 67% of Australian women in residential care had 25(OH)D levels below 10ng/ml³

References:
1. Le Boff M, JAMA 1999; 281:1505-11

Vitamin D

- Measure 25(OH)D (25-hydroxyvitamin D)¹
  - Current reference is > 20 ng/ml
  - Treatment target is ≥ 40 ng/ml
- Healthy individuals with levels of 20 ng/ml showed poor Ca⁺ absorption from a test meal.¹
- Individuals who are truly deficient will likely need large dosages of Vitamin D

References:
### Physical Examination Findings

- **Weight/Body Mass Index**
  - Weight < 127 pounds; BMI < 19 are risk factors
- **Obtain yearly height**
  - Compare heights from year to year
  - Ideally, measure heights with stadiometer
  - Loss of > 1.5 inch in lifetime is considered significant
  - Loss of > 1.0 inch in one year signifies possible fracture
- **Assess for dorsal kyphosis and cervical lordosis**
- **Palpate spine for tender or painful areas**
- **Assess for muscle strength and balance**

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### Additional Testing As Indicated to Rule-Out a Secondary Cause of Osteoporosis

- **CBC with differential**
  - Cancer
- **Comprehensive metabolic panel**
  - Renal or liver disease
  - Serum calcium
- **25 (OH) D**
  - Vitamin D deficiency
- **TSH and Free T4**
  - Hyperthyroidism
- **24-hour urine for calcium excretion**
- **Free testosterone level (both free and total)**
  - Hypogonadism
- **PTH**
  - Hyperparathyroidism

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### Diagnosis of Osteoporosis
Recognizing Osteoporosis: Usefulness of BMD Testing

• In clinical practice, BMD
  – Remains the gold standard\(^1\)
  – Is one of the best determinants of bone strength\(^2\)
  – Correlates with fracture risk\(^1,2\)

• BMD predicts fracture as reliably as blood pressure predicts stroke.\(^1,3\)


Diagnosis of Osteoporosis

• DXA Scan
  – Central DXA
  – Most accurate for serial measurements
  – Allows comparison between current and previous DXA scans


BMD Testing

• Recommended for:
  – Postmenopausal women ≥ 65 years of age
  – Men age ≥ 70 years
  – Postmenopausal women < 65 years of age with multiple osteoporotic risk factors
  – Men and women with fragility fractures
  – Men and women having diseases or using medications that can increase the risk of osteoporotic fractures

WHO Definition of T-Score

Anna (continued)

1. Does she meet the diagnostic criteria for osteopenia or osteoporosis?

   T scores:
   -1.7 Hip
   -2.0 L-S spine

Treatment Options
Summary of Revisions

• Treatment Recommendations
  – Treat all individuals with a T score of -2.5 in the hip
  – Those with T scores of -1.0 to -2.5 (osteopenia) should be treated when the 10 year probability of a hip fracture is $\geq$ 3% (FRAX® model) OR the 10 year probability of a major osteoporosis related fracture is $> 20\%$ based upon the US adapted WHO criteria (FRAX® model)

• FRAX®
  – WHO Fracture Risk Assessment Model/Tool
  – Provides 10 year probability of fracture risk
  – New risk assessment tool
Summary: Important To Remember…

- One-half or more of our fractures occur in individuals with T scores better than -2.5 SD.
- Thus, treating by BMD alone may not be the answer.
- Hence, the new revisions to the guidelines.

Nonpharmacologic Therapies

- Improved dietary calcium and vitamin D
- Exercise
  - Aerobic
  - Weight bearing
  - Increase muscle strength and flexibility
- Discontinue smoking
- Moderation of alcohol
- Avoidance of medications which increase risk
Calcium

- Calcium
  - The average woman in the United States consumes approximately 500mg of calcium daily.\(^1\)
  - Recommended daily amounts
    - Age 11-24: 1200 - 1500mg/day
    - During pregnancy: 1200mg/day
    - Age 25-50: 1000mg/day

Summary of Recent Revisions

- Calcium and Vitamin D recommendations
  - Calcium: 1200 mg per day for those over 50 years of age
  - Vitamin D\(_3\): 800 iu – 1000 iu per day for those over 50 years of age

Clinical Pearls with Calcium

- Calcium supplements should be taken with meals and in divided doses with no more than 500 mg – 600 mg at one time.
  - The fraction of the oral dose of calcium that is absorbed diminishes above this dose.\(^1\)
- If the patient is on a PPI (Proton Pump Inhibitor), use a citrate preparation.
  - Calcium carbonate needs an acidic environment to activate absorption.\(^2\)
- Viaactive contains vitamin K which may increase coagulability in patients taking anticoagulants.

\(^1\) Piper, BA, et. Al. Diagnosis and management of osteoporosis. Contemp Intern Med. 1995;7:61-68
Vitamin D

- Obtain in all individuals with osteopenia and osteoporosis
- Acts to enhance or facilitate the absorption of calcium from the gastrointestinal tract
- Recommended daily intake: 1000 iu
- Adults > 50 years - 1000 iu of Vitamin D daily

3. www.nof.org

Vitamin D Pearls

- Available by sunlight exposure
  - 5-10 minutes 3x/ week (face & arms)
  - Sunscreen blocks necessary UV exposure
- Available from 4 - 5 servings of liquid dairy products per day
- Patients in long-term care facilities should be considered for supplementation
- Vitamin D3 is preferred over D2

1. Food and Nutrition Board, Inst of Medicine 1997
2. Glowacki J, Curr Opin Endocr & Diabetes 2004

Vitamin D Requirements

- 3000-5000 IU used each day
- 1000 IU intake MINIMUM needed to satisfy daily needs

Reduction of Nonvertebral Fracture with Calcium and Vitamin D

% Fracture

Placebo
Calcium + Vitamin D

50% relative risk reduction

p=0.02


FDA Approved Medications of Use in Postmenopausal Osteoporosis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Prevention</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrogen/estrogen-progesterone</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Fosamax – alendronate</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Fosamax Plus D – alendronate sodium/cholecalciferol</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Boniva – ibandronate sodium tablets</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Boniva – ibandronate sodium injection</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Actonel – risedronate</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Actonel with Calcium – risedronate sodium tablets with calcium carbonate tablets, USP</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Evista – raloxifene</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Miacalcin – calcitonin</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Fortical – calcitonin-salmon (rDNA origin) nasal spray</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Forteo – teriparatide</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Reclast – zoledronic Acid</td>
<td>No</td>
<td>Yes</td>
</tr>
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</table>

Product Inserts

Two Primary Types of Pharmacotherapy for Osteoporosis

Antiresorptive Agents (reduce bone loss) | Anabolic Agents (build bone)

- Bisphosphonates
- Estrogen (HRT)
- Selective estrogen modulators (SERMS)
- Calcitonin

Bisphosphonates Are the Most Commonly Used Pharmacotherapy

- Most commonly prescribed medication class for osteoporosis with 200 million prescriptions written worldwide.¹
- Increase in BMD at the hip and spine²
- Reduce the risk of fractures²,³
- Have a demonstrated tolerability profile⁴


Oral Bisphosphonates…….

<table>
<thead>
<tr>
<th>Product</th>
<th>Alendronate Fosamax</th>
<th>Ibandronate Boniva</th>
<th>Risedronate Actonel</th>
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<tbody>
<tr>
<td>HT Study</td>
<td>Non-Vertebral Fracture</td>
<td>51-56%</td>
<td>69%</td>
</tr>
<tr>
<td>MOBILE Study</td>
<td>Vertebral Fracture</td>
<td>52%</td>
<td>52%</td>
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<tr>
<td>VERT Trial</td>
<td>L-S BMD</td>
<td>6.5%</td>
<td>6.6%</td>
</tr>
<tr>
<td></td>
<td>Fem Neck BMD</td>
<td>5.9%</td>
<td>2.8%</td>
</tr>
<tr>
<td></td>
<td>Side Effects</td>
<td>Dyspepsia</td>
<td>Joint Pain</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cost</td>
<td>Generic</td>
<td>Generic</td>
</tr>
</tbody>
</table>

Results are not from head to head clinical trials – comparisons of efficacy should not be made.

What About Patients Who Are Intolerant of Oral Therapies?

- Ibandronate (Boniva) I.V. Injection
  - FDA approved for the treatment of postmenopausal osteoporosis in women unable to tolerate oral regimens
  - Administered once every 3 months
  - 3 mg/every 3 months
    • Slow IV push (15 – 30 second injection)
  - Obtain creatinine prior to administration

Zoledronic Acid (Reclast)
Bisphosphonate Derivative

- Indications: Treatment of postmenopausal osteoporosis
- Dosing: 5mg IV every 12 months
- Infuse over 15-30 min; do not infuse < 15 minutes
  - Dilute solution for injection in 100 mL NS or D5W prior to administration (good hydration prior to giving)
- Excretion:
  - Urine 39% as unchanged drug within 24 hours

Zoledronic Acid (Reclast) – 3-year Clinical Fracture Data

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Reclast N=3875 Event Rate N (%)</th>
<th>Placebo N=3861 Event Rate N (%)</th>
<th>Absolute Reduction in Fracture Incidence</th>
<th>Relative Risk Reduction in Fracture Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Clinical Fracture</td>
<td>308 (8.4)</td>
<td>456 (12.8)</td>
<td>4.4 (3.0)</td>
<td>33 (23.0)</td>
</tr>
<tr>
<td>Clinical Vertebral Fracture</td>
<td>19 (0.5)</td>
<td>84 (2.6)</td>
<td>2.1 (1.5)</td>
<td>77 (63.0)</td>
</tr>
<tr>
<td>Non vertebral Fracture</td>
<td>292 (8.0)</td>
<td>388 (10.7)</td>
<td>2.7 (1.4)</td>
<td>25 (13.0)</td>
</tr>
</tbody>
</table>

Zoledronic Acid (Reclast) Bisphosphonate Derivative

- Renal impairment:
  - Creatinine Clearance of < 35mL/min - not recommended.
- Side Effects:
  - Fatigue (39%)
  - Fever (32-44%)
  - Headache (5-19%)
  - Dizziness (18%)
  - Anxiety, insomnia, depression (11-14%)
Bone, Joint and/or Musculoskeletal pain

- The product inserts for all of the bisphosphonates have a warning about bone, joint, and/or musculoskeletal pain.
- MedWatch safety summary suggests the association between bisphosphonates and musculoskeletal pain may be overlooked by healthcare professionals
  - Delaying diagnosis
  - Prolonging pain and/or impairment
  - Necessitating the use of analgesics

[Link to MedWatch summary](http://www.fda.gov/medwatch/safety/2008/safety08.htm#bisphosphonates) Accessed 01-07-08

<table>
<thead>
<tr>
<th>Other Therapies</th>
<th>Product</th>
<th>Raloxifene HCL</th>
<th>Calcitonin</th>
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<tbody>
<tr>
<td></td>
<td>Evista</td>
<td>ns</td>
<td>48%</td>
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<tr>
<td>Non-Vertebral Fracture</td>
<td>55%</td>
<td>36%</td>
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<tr>
<td>Vertebral Fracture</td>
<td>2.6%</td>
<td>Not available</td>
<td></td>
</tr>
<tr>
<td>L-S BMD</td>
<td>2.1%</td>
<td>Not available</td>
<td></td>
</tr>
<tr>
<td>Femoral Neck BMD</td>
<td>Oral</td>
<td>Intranasal</td>
<td></td>
</tr>
<tr>
<td>Route</td>
<td>Thromboembolism</td>
<td>Nausea, Diarrhea</td>
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<tr>
<td>Side Effects</td>
<td>Hot Flashes</td>
<td>Flushing, Rhinorrhea</td>
<td></td>
</tr>
<tr>
<td>Cost</td>
<td>$71</td>
<td>$68</td>
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</tr>
</tbody>
</table>

Denosumab

- **Denosumab: Prolia**
- **Class:** RANK ligand (receptor activator of nuclear factor Kappa –B ligand)
  - Human IgG2 monoclonal antibody with affinity and specificity for human RANKL
  - Produced from genetically engineered mammalian (Chinese hamster ovary) cells

[Wright, 2018](#)
Denosumab

► Indication:
  – Postmenopausal women with osteoporosis at high risk for fracture
► Dosage:
  – 60 mg administered as a single subcutaneous injection – every 6 months
  – Administer into upper arm, upper thigh, or the abdomen

Denosumab

► Contraindications:
  – Hypocalcemia
► Warnings and precautions:
  – Hypocalcemia can be exacerbated by denosumab
  – Serious infections
    ▶ 7800 patients in trial; infections were more common in individuals treated with this medications
    ▶ 3.3% in the placebo group; 4.0% in the treatment group
    ▶ Endocarditis: 0 – placebo; 3 in denosumab group

Why Potential for Infection?

► RANKL (receptor activator of nuclear factor Kappa –B ligand) is expressed on T and B lymphocytes and in lymph nodes
► RANKL inhibitor may increase risk of infection
Denosumab

► Warnings and precautions
  – ONJ
  – Dermatologic adverse reactions
    ▶ 2.0% placebo
    ▶ 2.5% denosumab
  – Pancreatitis - higher rates
  – Renal impairment: no dosage adjustment needed

Efficacy

► New vertebral fractures
  – Placebo: 7.2%
  – denosumab: 2.3% (ARR: 4.8%, RR reduction: 68%)

► Hip fractures
  – Placebo: 1.2%
  – denosumab: 0.7% (ARR: 0.3%, RRR: 40%)
  – All at year 3

► Improvement in bone density over 3 years:
  – 8.8% - Lumbar spine
  – 6.4% - Total hip
  – 5.2% - Femoral neck
### Additional Indication

- **Denosumab (XGEVA)**
- Prevention of skeletal-related events (SREs) in patients with bone metastases from solid tumors (i.e. prostate cancer)
- Competition: zoledronic acid (Zometa)

### Teriparatide (Forteo)

- **Indications:**
  - Treatment of postmenopausal women with osteoporosis who are at high risk for fracture
  - Women who have failed or are intolerant of previous osteoporosis therapy
  - Men with primary or hypogonadal osteoporosis who are at high risk for fracture
- **Dosage:**
  - Subcutaneous injection into the thigh or abdominal wall
  - Recommended dosage: 20 mcg once a day for up to 2 years
- **Side effects:**
  - Pain at injection site, arthralgias
  - Check serum calcium

### Trabecular Connectivity

- 64 year old woman treated with teriparatide

![Before](image1.png)  
![After](image2.png)

Abaloparatide (Tymlos)

- **Class:**
  - A human parathyroid hormone related peptide analog
- **Indication:**
  - Treatment of postmenopausal women with osteoporosis at high risk for fracture
- **Dosage:**
  - 80 mcg subcutaneously once daily
  - Subcutaneous injection into periumbilical region of abdomen


Abaloparatide

- **Warnings and Precautions**
  - Instruct patients to lie down during administration due to reports of orthostatic symptoms (for first few doses)
  - Avoid in patients with hypercalcemia
  - Osteosarcoma (rats/mice): class label
  - Not recommended in individuals with Paget’s disease
  - Limit use to 2 years


Abaloparatide

- **Efficacy:**
  - 1139 patients exposed to medication over 18 – 25 months
  - Increased BMD (8.8% vertebral spine, 3.5% hip)
  - Significant reduction in new vertebral fractures (0.6%, compared to 4.2% placebo, p <0.0001) and non-vertebral fractures
- **Drug – drug interactions:** NONE
- **Competition:**
  - Teriparatide (Forteo)

Abaloparatide

• Side effects
  – Hypercalciuria (11% vs. 9%)
  – Dizziness (10% vs. 6%)
  – Nausea (8% vs. 3%)
  – Headache (8% vs. 6%)
  – Injection site reactions (58% vs. 28%)

• Lab changes:
  – Increase in calcium
  – Increase in uric acid


Abaloparatide

• Advantages:
  – No dosage adjustment for mild – severe renal disease

• Disadvantages:
  – Cost (approximately $1600.00 per month)
  – Subcutaneous injection
  – Store in refrigerator


Re-evaluation after therapy

• Monitoring of therapy has traditionally been with BMD every two years
• Remember: One does not need to show gains in BMD to have success
• However, continuing loss suggests secondary cause or poor adherence
• Perhaps the increasing accuracy of biochemical markers will allow more rapid patient assessment, with three to six month values likely predictive of future BMD change.

Osteonecrosis of the Jaw (ONJ)

• Characterized clinically by an area of exposed bone in the mandible, maxilla or palate that typically heals poorly or does not heal over a period of 6 to 8 weeks.¹
• ONJ has occurred in one in 100,000 individuals on oral bisphosphonates.²
• 95% of ONJ is related to IV bisphosphonates for cancer therapy.²


Osteonecrosis of the Jaw

• 60% of those with ONJ had a recent dental extraction as a predisposing factor.
  – The majority have an underlying malignancy as an added risk.
• In general, ONJ rates in these patients range from 1.3% to 7%.


Osteonecrosis of the Jaw

• Predisposing factors for the development of ONJ appear to be
  – Dental surgery
  – Oral trauma
  – Periodontitis
  – Poor dental hygiene
  – Treatment with chemotherapy
  – Treatment with corticosteroids

How should clinicians respond?

- The documented benefits from the use of bisphosphonates for established indications clearly outweigh whatever small risk of ONJ documented in the literature.
- For the patient on nitrogen-containing bisphosphonates caution should be used in recommending elective invasive dental work such as dental-implant surgery.

Pulse Therapy

- Women who discontinued alendronate after 5 years showed:
  - A moderate decline in BMD
  - A gradual rise in biochemical markers
  - No higher hip fracture risk (although slightly higher clinical vertebral fractures) compared to those who continued alendronate
- Results suggest that for many women, discontinuation of alendronate for up to 5 years does not appear to significantly increase fracture risk.
- Can we do this clinically?

Case Study
Case Study
Anna: 57-year-old female

- Family History
  - Mother with hip fracture at age 75
  - Sister with vertebral fractures age 58

- PMH
  - No personal history of fractures (fragility or traumatic)
  - Hypothyroid with replacement (TSH - 0.89)
  - Asthma – present since childhood
  - TAH/BSO at age 40
  - Hypertension – diagnosed at age 46

Anna (continued)

- Social History
  - 2 oz white wine daily for past 10 years
  - Smoker – 15 pack year history of smoking
    - Discontinued 10 yrs ago; no relapses
  - Exercise:
    - Walks 1 mile daily - 20 minutes approximately 4 times per week

- Medications
  - Levothyroxine 125 mcg one po daily for 20 years
  - HCTZ 12.5 mg one po daily
  - Prednisone (medrol dose pack) 4 – 5 times yearly
  - Advair 250/50 mcg 1 puff twice daily

Anna (continued)

- Physical Examination
  - 65 inches
  - 111 pounds

- Labs
  - 25 (OH) Vitamin D Level: 21.5
  - Serum Calcium: 8.9

- DXA Scan
  - Hip: T Score = -1.7
  - LS spine: T Score = -2.0
Anna (continued)

1. Would you treat Anna?
2. If yes, with what?
   a. Calcium and vitamin D
   b. ET/HT
   c. SERM
   d. Calcitonin
   e. Bisphosphonate (weekly, monthly, every 3 months, once yearly)
   f. Parathyroid hormone

Summary

• Osteoporosis is underdiagnosed and undertreated.
• Numerous options exist to treat and prevent this condition
• Adherence to any chronic medication is often poor. Therefore, all techniques to improve outcomes should be entertained.

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