Osteoporosis Screenings and Upcoming Osteoporosis Medications
Screening Tools, Prevention, and New Medications in the Pipeline

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Assistant Professor (Clinical)

Disclosures

- Mary Beth O’Connell, Pharm.D. and Joseph Fava, Pharm.D. declare no conflicts of interest, real or apparent, and no financial interests in any company, product, or service mentioned in this program, including grants, employment, gifts, stock holdings, and honoraria.

Learning Objectives - Pharmacists

- Interview patients to estimate their osteoporosis fracture risk and determine their calcium and vitamin D needs
- Explain the pharmacology and role of agents from two new medication classes of osteoporosis medications
- Compare romosozumab and abaloparatide to current prescription OP medications

Learning Objectives – Pharmacy Technicians

- Know the types of data needed to be gathered to estimate a patient’s 10-year osteoporotic fracture risks
- Explain toxicity from excessive calcium intake
- Understand two new osteoporosis medications
  - Abaloparatide
  - Romosozumab

Osteoporosis Cases

- Please read the two cases. We will be using these cases throughout the presentation
  - Case 1: Ms. Ling – postmenopausal woman
- Write down your answers to the case questions as we go along

Osteopenia and Osteoporosis: Epidemiology (U.S. Data)

- Prevalence
  - 44 million with osteopenia
  - 10 million with osteoporosis
- Gender differences - osteoporosis
  - Women: 80%
- Prevalence by race/ethnicity (women > 50 years old)
  - Caucasian: 20%
  - Asian American: 20%
  - Latina: 10%
  - Non-Hispanic African American: 5%
- Expensive - $19 billion annually, $25.3 billion by 2025

https://www.nof.org/
Osteoporotic Fractures

- 8.9 million fractures annually worldwide
- In U.S.
  - About 1 in 2 women ≥ 50 years
  - About 1 in 4 men > 50 years
- Hip fractures
  - 10-20% require long-term nursing care
  - 60% have independency limitations
  - 20-24% die within a year
  - Mortality rate men > women

Screening for Osteoporosis and Fracture Risk: Patient Assessments

- Screening
  - Annual height
  - FRAX
- Diagnosis
  - DXA
    - T-score (young adult, sex reference)
    - Z-score (age, sex, race, ethnicity reference)
  - Vertebral imaging
- Secondary causes/risk factors
- Monitoring
  - DXA
  - Biomarkers (osteocalcin, bone-specific AP, CTX, NTX)

Height Measurements

- Annual assessment
- Preferably with stadiometer
  - Heels, buttock and shoulder blades touch wall
  - Line of vision parallel to floor
- Significant loss
  - Overall (since peak at age 20):
    - > 1.5 inch loss
  - Prospective (since a previously documented measurement):
    - > 0.8 inch loss

Fracture Risk Assessment Tool (FRAX)

- Developed by the World Health Organization (WHO) task force in 2008
  - Prediction tool
  - Assesses fracture risk
  - Provides general guidance for screening and treatment decisions
  - Estimates country and race/ethnicity-specific 10-year risk of
    - Major osteoporotic fracture
    - Hip fracture
- Valid in
  - Postmenopausal women
  - Men
  - Anyone with osteopenia
- INVALID if on Rx medication(s) for OP***

Osteoporosis Guidelines: Prevention and Treatment

<table>
<thead>
<tr>
<th>Organization</th>
<th>Title</th>
<th>Year Published</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE)</td>
<td>Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis</td>
<td>2016</td>
</tr>
<tr>
<td>U.S. Preventative Services Task Force (USPSTF)</td>
<td>Screening for Osteoporosis: USPSTF Recommendation Statement</td>
<td>2011</td>
</tr>
<tr>
<td>U.S. Preventative Services Task Force (USPSTF)</td>
<td>Osteoporotic Fractures: Screening</td>
<td>2017 (In progress)</td>
</tr>
<tr>
<td>International Society of Clinical Densitometry (ISCD)</td>
<td>Indications for Bone Mineral Density (BMD) Testing</td>
<td>2013</td>
</tr>
<tr>
<td>Endocrine Society</td>
<td>Osteoporosis in Men: An Endocrine Society Clinical Practice Guideline</td>
<td>2012</td>
</tr>
<tr>
<td>U.S. Preventative Services Task Force (USPSTF)</td>
<td>Screening for Vitamin D Deficiency in Adults: USPSTF Recommendation Statement</td>
<td>2014</td>
</tr>
</tbody>
</table>

RF for OP ➔ Indication for vertebral imaging

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Using the FRAX Tool – Collecting Risk Factors

"Do you regularly take any steroid type medications like prednisone, cortisone, or dexamethasone?"

Using the FRAX Tool – Clarifying Risk Factors

Rheumatoid Arthritis
- Autoimmune chronic inflammatory polyarthritis (arthritis that affects 5 or more joints)
- Older adults often confuse with osteoarthritis
  - Breakdown of cartilage leading to pain, stiffness and swelling
- Confirmation:
  - “Do you have, or have you ever been told by a healthcare provider that you have rheumatoid arthritis?”

Rheumatoid Arthritis Therapies
- NSAIDs
- Steroids
- DMARDs
  - Methotrexate
  - Leflunomide (Arava)
  - Hydroxychloroquine (Plaquenil)
  - Sulfasalazine (Azulfidine)
- Biologics
  - Abatacept (Orencia)
  - Adalimumab (Humira)
  - Anakinra (Kineret)
  - Certolizumab (Cimzia)
  - Etanercept (Enbrel)
  - Golimumab (Simponi)
  - Infliximab (Remicade)
  - Rituximab (Rituxan)
  - Tocilizumab (Actemra)
  - Tofacitinib (Xeljanz)
Using the FRAX Tool – Collecting Risk Factors

Calculation Tool
Please answer the questions below to calculate the 10-year probability of fracture with FRAX.

<table>
<thead>
<tr>
<th>Questionnaire</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Is the patient 50 years of age or older?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>2. Has the patient ever had a fracture?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>3. Does the patient currently use glucocorticosteroids?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>4. Has the patient undergone a bone density test within the past 5 years?</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Height Conversion
<table>
<thead>
<tr>
<th>Unit</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>m</td>
<td></td>
</tr>
<tr>
<td>cm</td>
<td></td>
</tr>
</tbody>
</table>

Using the FRAX Tool – Clarifying Risk Factors

Bone Density: Dual-Energy Absorptiometry (DXA)

- Appropriate for screening, diagnosis, and monitoring
- Spine, femoral neck, total hip
  - Non-fractured hip
- Minimal radiation
- Sites with quality assurance programs
- Preferably use same machine at same site for repeat measures
- Lowest value for interpretation

DXA T-score and Z-score Interpretations

<table>
<thead>
<tr>
<th>T-score (SD)*</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; -1</td>
<td>Normal</td>
</tr>
<tr>
<td>-1.0 to -2.5</td>
<td>Low bone mass (osteopenia)</td>
</tr>
<tr>
<td>≤ -2.5**</td>
<td>Osteoporosis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Z-score (SD)</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; -2.0</td>
<td>Within the expected range for age</td>
</tr>
<tr>
<td>≤ -2.0</td>
<td>Below the expected range for age</td>
</tr>
</tbody>
</table>

*SD = standard deviation for female Caucasian reference range for everyone
**WHO International standard for diagnosis is score at femoral neck
Using the FRAX Tool – Collecting Risk Factors

If YES – Select T-score, enter and calculate
If NO – Leave blank and calculate

Post-FRAX Results
Indications for DXA

<table>
<thead>
<tr>
<th>Gender</th>
<th>Indication(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>&gt; 65 YO (NOF)</td>
</tr>
<tr>
<td></td>
<td>50-64 YO with FRAX major OP fracture risk ≥ 0.3% based on FRAX (USPSTF)</td>
</tr>
<tr>
<td></td>
<td>Postmenopausal based on risk factors (NOF)</td>
</tr>
<tr>
<td></td>
<td>Low body weight</td>
</tr>
<tr>
<td></td>
<td>Prior fracture</td>
</tr>
<tr>
<td></td>
<td>Treatment use</td>
</tr>
<tr>
<td></td>
<td>Disease or condition associated with bone loss</td>
</tr>
<tr>
<td>Men</td>
<td>&gt; 70 YO (NOF)</td>
</tr>
<tr>
<td></td>
<td>50-64 YO based on risk factors (NOF)</td>
</tr>
<tr>
<td></td>
<td>Low body weight</td>
</tr>
<tr>
<td></td>
<td>Prior fracture</td>
</tr>
<tr>
<td></td>
<td>High risk medication use</td>
</tr>
<tr>
<td></td>
<td>Disease or condition associated with bone loss</td>
</tr>
</tbody>
</table>

Post-FRAX Results: OP Treatment

Recommended if***:

10-year probability of ANY major fracture ≥ 20%
- OR -
10-year probability of HIP fracture ≥ 3%

***TREATMENT decision will usually factor in history of fracture, T-score, clinical judgment, individual patient factors, and medication insurance

FRAX Validity – Current/Past OP Treatment

Situation | Valid? |
----------|--------|
Current/past use of calcium/vitamin D supplementation | YES |
Currently taking bisphosphonate, estrogen agonist/antagonist, calcitonin, synthetic PTH, or immunologic | NO |
Past OP treatment but off for 1-2 years | YES*** |

***Per NOF 2014: clinical judgment required, “might be considered untreated”

Disease and Drug Risk Factors

<table>
<thead>
<tr>
<th>Situation</th>
<th>Valid?</th>
</tr>
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<tbody>
<tr>
<td>Current/past use of calcium/vitamin D supplementation</td>
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<tr>
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**DXA for Screening and Therapy Monitoring**

- Follow-up screenings
  - No more than once every 2 years per AAFP
  - May wait longer for those with
    - No risk factors
    - Normal T-score
    - Clinical judgment

- OP therapy monitoring
  - 1 to 2 years after initiation and then every 2 years per clinical judgment
  - Preferred with same machine at same center
  - Change greater than the least significant change (LSC)
    - Machine dependent
    - ≈ 3% - 6% hip
    - ≈ 2% - 4% lumbar spine

**Case 1: OP and Fracture Risk Assessment**

- Ms. Ling
- What are her FRAX scores?
- Are they valid?
- Would you recommend DXA at this time?

How can she reduce her risk?
1. Bone healthy lifestyle
2. Adequate intakes of calcium and vitamin D

**Bone Healthy Lifestyle, Calcium and Vitamin D**

- Exercise: Aerobic, strengthening, and/or balancing exercises result in less bone loss
- Tobacco: Avoid
- Alcohol: Minimal (1/day women, 2/day men)
- Caffeine: Minimal
- Fall Risk: Home safety assessment, balance exercises, vitamin D assessment, avoidance of high-risk meds
- Calcium: Adequate intake per Institute of Medicine (IOM)
- Vitamin D: Adequate intake per IOM/NOF

**Bone Healthy Lifestyle**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Goal</th>
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<tr>
<td>Exercise</td>
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<td>Avoid</td>
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<tr>
<td>Alcohol</td>
<td>Minimal (1/day women, 2/day men)</td>
</tr>
<tr>
<td>Caffeine</td>
<td>Minimal</td>
</tr>
<tr>
<td>Fall Risk</td>
<td>Home safety assessment, balance exercises, vitamin D assessment, avoidance of high-risk meds</td>
</tr>
<tr>
<td>Calcium</td>
<td>Adequate intake per Institute of Medicine (IOM)</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Adequate intake per IOM/NOF</td>
</tr>
</tbody>
</table>

**Calcium and Bone Health**

- Most abundant mineral in body
- <1%: Vascular and muscle function, Nerve transmission, IC signaling, Hormone secretion
- 99%: Stored in bones and teeth, Constant resorption and deposition based on body needs

**IOM 2010 Calcium Allowances**

(from diet AND supplements)

<table>
<thead>
<tr>
<th>Category</th>
<th>Age</th>
<th>Calcium (mg)</th>
<th>Upper Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants</td>
<td>0–6 mo</td>
<td>200</td>
<td>1000</td>
</tr>
<tr>
<td></td>
<td>6–12 mo</td>
<td>260</td>
<td>1500</td>
</tr>
<tr>
<td>Children</td>
<td>1–3 yo</td>
<td>700</td>
<td>2500</td>
</tr>
<tr>
<td></td>
<td>4–8 yo</td>
<td>1,000</td>
<td>2500</td>
</tr>
<tr>
<td></td>
<td>9–18 yo</td>
<td>1,300</td>
<td>3000</td>
</tr>
<tr>
<td>Adults</td>
<td>19–50 yo</td>
<td>1,000</td>
<td>2500</td>
</tr>
<tr>
<td>Men</td>
<td>51–70 yo</td>
<td>1,000</td>
<td>2000</td>
</tr>
<tr>
<td>Woman</td>
<td>51–70 yo</td>
<td>1,200</td>
<td>2000</td>
</tr>
<tr>
<td>Woman and Men</td>
<td>&gt; 70 yo</td>
<td>1,200</td>
<td>2000</td>
</tr>
</tbody>
</table>

Note: Intakes > 1200 - 1500 mg increases risk for kidney stones, cardiovascular disease and stroke (2014 NOF guidelines)***
Calcium Intakes: NHANES 2003 - 2006 Database

<table>
<thead>
<tr>
<th>Age</th>
<th>Adequate Intakes</th>
<th>Dietary Intake Use (%)</th>
<th>Supplement Use (%)</th>
<th>Adequate Intakes</th>
<th>Dietary Intake Use (%)</th>
<th>Supplement Use (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>19 – 30</td>
<td>1000</td>
<td>686</td>
<td>34</td>
<td>1000</td>
<td>942</td>
<td>42</td>
</tr>
<tr>
<td>31 – 40</td>
<td>1000</td>
<td>730</td>
<td>43</td>
<td>1000</td>
<td>908</td>
<td>50</td>
</tr>
<tr>
<td>41 – 50</td>
<td>1000</td>
<td>571</td>
<td>47</td>
<td>1000</td>
<td>832</td>
<td>56</td>
</tr>
<tr>
<td>51 – 60</td>
<td>1200</td>
<td>649</td>
<td>50</td>
<td>1200</td>
<td>777</td>
<td>66</td>
</tr>
<tr>
<td>61 – 70</td>
<td>1200</td>
<td>641</td>
<td>55</td>
<td>1200</td>
<td>758</td>
<td>70</td>
</tr>
<tr>
<td>71 – 80</td>
<td>1200</td>
<td>633</td>
<td>56</td>
<td>1200</td>
<td>725</td>
<td>64</td>
</tr>
<tr>
<td>≥ 80</td>
<td>1200</td>
<td>589</td>
<td>54</td>
<td>1200</td>
<td>708</td>
<td>64</td>
</tr>
</tbody>
</table>

Dietary Sources of Calcium

<table>
<thead>
<tr>
<th>Product</th>
<th>Serving Size</th>
<th>Approximate calcium content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>1 cup</td>
<td>300</td>
</tr>
<tr>
<td>Yogurt (low fat or plain)</td>
<td>8 oz</td>
<td>343-415</td>
</tr>
<tr>
<td>Kale (cooked)</td>
<td>1 cup</td>
<td>90</td>
</tr>
<tr>
<td>Cheese (cheddar)</td>
<td>1 1/2 cups</td>
<td>306</td>
</tr>
<tr>
<td>Cottage cheese (1/2 milk fat)</td>
<td>1 cup</td>
<td>108</td>
</tr>
<tr>
<td>Salmon (pink, canned)</td>
<td>3 oz</td>
<td>181</td>
</tr>
<tr>
<td>Broccoli (raw)</td>
<td>1/2 cup</td>
<td>24</td>
</tr>
</tbody>
</table>

Dietary Calcium Intake Workup

- NOF Calcium Intake Estimator
  - https://www.nof.org/patients/treatment/calciumintake-calculator/
  - Estimate foods from other non-calcium rich sources

- International Osteoporosis Foundation (IOF) Calcium Calculator
  - https://www.iofbonehealth.org/calcium-calculator
  - Accounts for almost all foods in diet

Supplemental Calcium Intake Workup

<table>
<thead>
<tr>
<th>Product Type</th>
<th>Product Name</th>
<th>Directions</th>
<th>Elemental Calcium (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nutritional</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supplement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other (calcium-based antacids, etc.)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Calcium and Food Labels

RDA of Calcium: 1000 mg (per 1500 kcal)

\[
x = 0.35 \\
= \frac{350}{1000} = 0.35 (per 8 oz serving)\]
### Supplemental Calcium Intake Workup: Example: Floyd

**Medications:**
- Actoplus Met 45/500 mg – 1 tablet BID
- HCTZ 25 mg – 1 tablet daily
- Simvastatin 40 mg – 1 tablet QHS
- Tramadol 50 mg – 1 tablet BID PRN
- Tums® Extra Strength 750 – 1-2 tablets 2-4x/week PRN for heartburn
- Centrum® Silver® Men – 1 tablet daily

<table>
<thead>
<tr>
<th>Product type</th>
<th>Product name</th>
<th>SIG</th>
<th>Elemental Calcium (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamin</td>
<td>Centrum® Silver® Men</td>
<td>1 tablet daily</td>
<td>???</td>
</tr>
<tr>
<td>Nutritional supplement</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Calcium supplement</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Other (calcium-based antacids, etc.)</td>
<td>Tums® Extra Strength 750</td>
<td>1-2 tablets 2-4x/week PRN for heartburn</td>
<td>???</td>
</tr>
</tbody>
</table>

---

**How do you interpret drug fact labeling for calcium content?**

- Calcium Salts
  - Calcium available in MVIs and supplements vary in salt type
  - Calcium carbonate = 40% elemental calcium
  - Calcium citrate = 21% elemental calcium
  - Calcium gluconate = 9% elemental calcium
  - Calcium lactate = 13% elemental calcium

---

### Total Calcium Intake Workup Example: Floyd

**Medications:**
- Actoplus Met 45/500 mg – 1 tablet BID
- HCTZ 25 mg – 1 tablet daily
- Simvastatin 40 mg – 1 tablet QHS
- Tramadol 50 mg – 1 tablet BID PRN
- Tums® Extra Strength 750 – 1-2 tablets 2-4x/week PRN for heartburn
- Centrum® Silver® Men – 1 tablet daily

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<tr>
<th>Product type</th>
<th>Product name</th>
<th>SIG</th>
<th>Elemental Calcium (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamin</td>
<td>Centrum® Silver® Men</td>
<td>1 tablet daily</td>
<td>210</td>
</tr>
<tr>
<td>Nutritional supplement</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Calcium supplement</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Other (calcium-based antacids, etc.)</td>
<td>Tums® Extra Strength 750</td>
<td>1-2 tablets 2-4x/week PRN for heartburn</td>
<td>214</td>
</tr>
</tbody>
</table>

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**Calcium and Supplement Labels**

- Salt form not given – how do I calculate?
  - No need when % DV is given – always represents elemental amount

---

**Calcium and Drug Labels**

- No % DV but salt given
  - 750 mg x 0.4 = 300 mg/tablet

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**Common mistakes**

- **CITRACAL® Petites**
  - Directions: Adults: Take 1 serving (2 tablets) twice daily with or without food or as recommended by your physician, pharmacist or healthcare professional.
  - Supplement Facts
    - Serving Size: 2 tablets
    - Servings Per Container: Net Qty Contents/Serving Size (6 tablets)
    - Amount Per Serving
      - Vitamin D (as cholecalciferol): 500 IU
      - Calcium (elemental): 400 mg
      - Total: 424
  - INGREDIENTS: Calcium Citrate, Polyethylene Glycol, etc.
Common Mistakes

- Tricky Labeling
- Sentry Senior MVI

Always go by % DV


Calcium Supplements Adverse Effects

<table>
<thead>
<tr>
<th>Incidence</th>
<th>Severity</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common</td>
<td>Mild</td>
<td>Gas, bloating, flatulence, Constipation (mostly with carbonate)</td>
</tr>
<tr>
<td>Less common</td>
<td>Moderate</td>
<td>Abdominal pain, nausea (Typically when doses &gt; 500 mg taken at once)</td>
</tr>
<tr>
<td>Rare</td>
<td>Severe</td>
<td>Hypercalcemia, Nephrocalcinosis, Hypophosphatemia, Metabolic alkalosis</td>
</tr>
</tbody>
</table>

Bone Healthy Lifestyle

<table>
<thead>
<tr>
<th>Factor</th>
<th>Goal</th>
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<tbody>
<tr>
<td>Exercise</td>
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<td>Caffeine</td>
<td>Minimal</td>
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<td>Full Risk</td>
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</tr>
<tr>
<td>Vitamin D</td>
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</tbody>
</table>

Vitamin D and Bone Health

Vitamin D: Dietary Sources

<table>
<thead>
<tr>
<th>Food</th>
<th>400 IU</th>
<th>600 IU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cod liver oil, 1 tablespoon</td>
<td>1360</td>
<td>2040</td>
</tr>
<tr>
<td>Swordfish, cooked, 3 ounces</td>
<td>566</td>
<td>849</td>
</tr>
<tr>
<td>Salmon (sockeye), cooked, 3 ounces</td>
<td>447</td>
<td>671</td>
</tr>
<tr>
<td>Tuna fish, canned in water, drained, 3 ounces</td>
<td>154</td>
<td>231</td>
</tr>
<tr>
<td>Orange juice fortified with vitamin D, 1 cup (check product labels, as amount of added vitamin D varies)</td>
<td>137</td>
<td>205</td>
</tr>
<tr>
<td>Milk, nonfat, reduced fat, and whole, vitamin D-fortified, 1 cup</td>
<td>115-124</td>
<td>172-187</td>
</tr>
<tr>
<td>Yogurt, fortified with 20% of the DV for vitamin D, 6 ounces (more heavily fortified yogurts provide more of the DV)</td>
<td>80</td>
<td>120</td>
</tr>
<tr>
<td>Margarine, fortified, 1 tablespoon</td>
<td>60</td>
<td>90</td>
</tr>
<tr>
<td>Sardines, canned in oil, drained, 2 sardines</td>
<td>46</td>
<td>69</td>
</tr>
<tr>
<td>Liver, beef, cooked, 3 ounces</td>
<td>42</td>
<td>63</td>
</tr>
<tr>
<td>Egg, 1 large (vitamin D is found in yolk)</td>
<td>41</td>
<td>62</td>
</tr>
<tr>
<td>Ready-to-eat cereal, fortified with 10% of the DV for vitamin D, 0.75-1 cup (more heavily fortified cereals might provide more of the DV)</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>Cheese, Swiss, 1 ounce</td>
<td>6</td>
<td>9</td>
</tr>
</tbody>
</table>

IOM 2010 Vitamin D Allowances

From Diet AND Supplements

<table>
<thead>
<tr>
<th>Category</th>
<th>Age</th>
<th>Vitamin D (units)</th>
<th>Upper Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants</td>
<td>0-6 mo</td>
<td>400</td>
<td>1000</td>
</tr>
<tr>
<td></td>
<td>6-12 mo</td>
<td>400</td>
<td>1500</td>
</tr>
<tr>
<td>Children</td>
<td>1-3 yo</td>
<td>600</td>
<td>2500</td>
</tr>
<tr>
<td></td>
<td>4-8 yo</td>
<td>600</td>
<td>3000</td>
</tr>
<tr>
<td></td>
<td>9-18 yo</td>
<td>600</td>
<td>4000</td>
</tr>
<tr>
<td>Adults</td>
<td>19-50 yo</td>
<td>600</td>
<td>4000</td>
</tr>
<tr>
<td></td>
<td>Men</td>
<td>51-70 yo</td>
<td>600</td>
</tr>
<tr>
<td></td>
<td>51-70 yo</td>
<td>600</td>
<td>4000</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>&gt; 70 yo</td>
<td>800</td>
</tr>
<tr>
<td></td>
<td>Women and Men</td>
<td></td>
<td>1000</td>
</tr>
</tbody>
</table>

RDA = 400 units

NOF: 800 – 1000 units/day in 50+

Vitamin D: Reference Intakes for Calcium and Vitamin D.
Dietary Vitamin D Intake Workup: Example: Floyd

65 YO Male

Diet:
- One glass of milk with breakfast most days
- One serving of cheese about 5 times per week
- Florida’s Natural Orange Juice with Calcium and Vitamin D – 1 glass 3-4x/week
- One to two servings of vegetables per day

120 units (diet) + 57 units (supplement) = Approximately 177 units/day

Supplemental Vitamin D Intake Workup: Floyd

Medications:
- Actoplus Met 15/500 mg – 1 tablet BID
- HCTZ 25 mg – 1 tablet daily
- Simvastatin 40 mg – 1 tablet bedtime
- Tramadol 50 mg – 1 tablet PRN
- Tums® Extra Strength 750 – 1-2 tablets 2-4x/week PRN for heartburn
- Centrum® Silver® Men – 1 tablet daily

Product type          Product name       Directions          Vitamin D (units/day)
Multivitamin          Centrum® Silver® Men
                      1 tablet daily       1000
Nutritional supplement – – – –
Calcium + D supplement – – – –
Vitamin D supplement  – – – –

Total: 177 units/day = Approximately 177 units/day

What if vitamin D concentration is low?

<table>
<thead>
<tr>
<th>Classification</th>
<th>Vitamin D Conc (ng/mL)</th>
<th>OTC Therapy (units)</th>
<th>Rx Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sufficient</td>
<td>&gt; 30 (NOF)</td>
<td>600-800 (IOM)</td>
<td>Vitamin D₃ daily</td>
</tr>
<tr>
<td></td>
<td>≥ 30 (ES)</td>
<td>1000-2000 (ES)</td>
<td>Vitamin D₂ or D₃</td>
</tr>
<tr>
<td>Insufficient</td>
<td>21 – 29 (21 – 30)</td>
<td>50,000 units/week</td>
<td>Vitamin D₂ or D₃</td>
</tr>
<tr>
<td></td>
<td>(21 – 30)</td>
<td>for 8–12 weeks or monthly</td>
<td></td>
</tr>
<tr>
<td>Deficient</td>
<td>≤ 20</td>
<td>6000 units daily</td>
<td>Vitamin D₂ or D₃</td>
</tr>
<tr>
<td></td>
<td></td>
<td>for 8–12 weeks or monthly</td>
<td></td>
</tr>
</tbody>
</table>

Simple Correction Algorithm

100 units/day → ↑ 1 ng/mL 25(OH) vitamin D

Calcium/Vitamin D Supplementation Controversies

- True efficacy of calcium + vitamin D supplementation in preventing or minimizing fractures
  - Proven in institutionalized older adults
  - Mixed evidence for 50+ community dwellers
  - Inadequate data for men and premenopausal women

Vitamin D Monitoring

- Baseline – 25(OH) vitamin D (optional)
  - Expensive test
  - Interlab variability
    - Vitamin D assay standards optional but suggested
- Monitoring
  - After 3 - 4 months of replenishment or maintenance therapy changes
  - Same laboratories

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### Calcium Supplementation: Controversies

- **Renal stones**
  - Most commonly composed of calcium oxalate (Ca salt of oxalic acid)
  - Some (but not all) studies suggest positive association between supplemental calcium and kidney stones
  - WHI: Risk increased 17%
  - NHS: Positive association w/ stone formation
  - High intakes of **dietary** calcium
    - No association w/ stones
    - May be protective
  - Likely higher risk with
    - High oxalate intake
    - Low fluid intake
  - High-oxalate foods
    - Spinach
    - Bran flakes
    - Rhubarb
    - Roots
    - Potato chips
    - French fries
    - Nuts and nut butters

### Calcium/Vitamin D Supplementation Controversies

- **Cardiovascular events**
  - Prospective studies are inconsistent
    - Many studies have shown ↑ risk, ↓ risk, or no association
  - Dietary effect vs. supplemental effect not clear
  - No established biological mechanism to support association
  - CVD outcomes often drawn from secondary analyses for trial data
  - American Society for Preventative Cardiology + NOF
    - 2021 meta-analysis of 4 randomized trials and 27 observational studies

### Calcium and Vitamin D Bottom Line

- **Achieve adequate intakes for overall health**
  - Preferably from diet
    - No ↑ risk stones, ↑ intake may be protective
    - No correlation to CV risk
  - Supplement only if needed to achieve IOM/NOF daily goals
    - Help patients understand labelled dosing recommendations
  - Vitamin D supplement to achieve therapeutic concentration of 20 – 30 ng/mL
    - Also prevents falls

### Case 1 Cont’d: Calcium/Vitamin D Assessment

- Ms. Ling
  - What are her daily calcium and vitamin D goals?
  - What are her approximated current daily intake of calcium and vitamin D?
  - What are your recommendations?

### Full Workup Template (WSU)

<table>
<thead>
<tr>
<th>Role of Formation Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Agent</td>
</tr>
<tr>
<td>Teriparatide (Forteo)</td>
</tr>
<tr>
<td>PTH moiety</td>
</tr>
<tr>
<td>Pending FDA Review</td>
</tr>
<tr>
<td>Abaloparatide</td>
</tr>
<tr>
<td>PTHrP peptide</td>
</tr>
<tr>
<td>Romosozumab (Evenity)</td>
</tr>
<tr>
<td>Antisclerostin</td>
</tr>
</tbody>
</table>
Cases
- Ms. Johnson: Chronic kidney disease
- Mr. Runninghorse: Very low BMD, Secondary osteoporosis
- Ms. Martindale: Osteoporosis fracture while on an antiresorptive medication

Osteoporosis Prescription Medications
- Current Classes
  - Antiresorption Meds
    - Bisphosphonates
    - RANKL inhibitors
    - Estrogen agonist/antagonist
    - Tissue selective estrogen complex
    - Calcitonin
    - Estrogens
  - Formation Meds
    - Initiation - PTH-like agents

- Awaiting FDA Approval
  - Antiresorption Meds
    - None
  - Formation Meds
    - PTHrP agents
    - Antisclerostin agents

2016 AACE and 2014 NOF Guidelines
Initiation of Pharmacologic Therapy
Postmenopausal Women and Men ≥ 50 yo
- History of vertebral or hip fracture
- T-score ≤ -2.5
  - DXA: femoral neck, total hip, OR spine
- Low bone mass (T-score -1.0 to -2.5) AND
  - 10-year probability of hip fracture ≥ 3% OR
  - 10-year probability of any major fracture ≥ 20%
  - Based on FRAX® estimations

American Association of Clinical Endocrinology (AACE)
Recommendations for Medication Use
- First line – hip and spine fracture prevention
  - Alendronate, risedronate, zoledronic acid for women & men
  - Denosumab for women
- Second line therapy – spine fracture prevention
  - Ibandronate, raloxifene
- Third line therapy
  - Raloxifene
- Fourth line therapy
  - Calcitonin
- Reserved for very high fracture risk or failed bisphosphonates
  - Teriparatide

Endo Pract 16:22 (Suppl 4):1-43

Multiple Medication Use
- NOF
  - Sequential preferred – formation agent then antiresorptive agent
    - Cost
    - Adversion to self-injection medications
  - Combination in select patients
    - Formation plus antiresorptive agent
- AACE
  - Sequential – yes
  - Combination – no fracture data
    - Ok if raloxifene for breast cancer prevention
    - Ok estrogens for menopause symptoms

Combination Therapy
Zoledronic Acid and Teriparatide
- Zoledronic Acid (ZOL)
- Teriparatide (TPTD)
- Combination (ZOL + TPTD)

J Bone Min Res 2011;26:909-11
Combination Therapy
Denosumab and Teriparatide

<table>
<thead>
<tr>
<th>Lumbar Spine BMD</th>
<th>Total Hip BMD</th>
<th>Distal 1/3 radius BMD</th>
</tr>
</thead>
<tbody>
<tr>
<td>-1.8</td>
<td>0.7</td>
<td>-0.7</td>
</tr>
<tr>
<td>2.5</td>
<td>4.9</td>
<td>2.5</td>
</tr>
<tr>
<td>9.1</td>
<td>6.2</td>
<td>5.5</td>
</tr>
</tbody>
</table>

Lancet 2013;382:50-6

Drug Holiday - AACE

- Moderate risk for osteoporotic fracture
  - Alendronate after 5 years
  - Zoledronic acid after 3 years
- Higher risk for osteoporotic fracture
  - Alendronate after 6 – 10 years
  - Zoledronic acid after 6 years
- During holiday for higher risk patients can use teriparatide or raloxifene
- Holiday duration unknown – monitor bone markers, BMD, and fractures
- No drug holiday for denosumab

Higher Risk

- Previous fracture
- Extremely low BMD (T-score ≤ -3.5)
- Multiple risk factors for fracture

Management of Osteoporosis in CKD

<table>
<thead>
<tr>
<th>eGFR (mL/min/1.73 m²)</th>
<th>Suggested Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;30 (CKD 1-3)</td>
<td>Biphosphonate therapy if no CKD-MBD</td>
</tr>
<tr>
<td>20-30 (CKD 4)</td>
<td>Consider bone biopsy to r/o CKD-MBD</td>
</tr>
<tr>
<td></td>
<td>“Off-label” PO biphosphonate - dose adjusted?</td>
</tr>
<tr>
<td></td>
<td>Raloxifene – not renally excreted</td>
</tr>
<tr>
<td></td>
<td>Denosumab – not renally excreted</td>
</tr>
<tr>
<td></td>
<td>Caution due to risk for hypocalcemia</td>
</tr>
<tr>
<td></td>
<td>Teriparatide if low or normal PTH</td>
</tr>
<tr>
<td>&lt;20 (CKD 5)</td>
<td>Bone biopsy recommended if considering osteoporosis therapy per KDIGO</td>
</tr>
<tr>
<td></td>
<td>Lack of evidence for any therapy choice</td>
</tr>
<tr>
<td></td>
<td>Unknown efficacy</td>
</tr>
<tr>
<td></td>
<td>Potential ↑ risk for complications</td>
</tr>
</tbody>
</table>

GIO Prevention and Treatment
Postmenopausal Women and Men > 50 yo

<table>
<thead>
<tr>
<th>≥ 3 mo</th>
<th>Low Risk</th>
<th>Medium Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FRAX &lt;10%</td>
<td>FRAX 10%-20%</td>
<td>FRAX &gt; 20%, T-score ≤ -2.5, or fragility fracture</td>
</tr>
<tr>
<td>Glucocorticoid</td>
<td>&lt; 7.5 mg/d</td>
<td>&lt; 7.5 mg/d</td>
<td>&lt; 5 mg/d ≤ 1 mo</td>
</tr>
<tr>
<td>No therapy</td>
<td>Alen, Ris</td>
<td>Alen, Ris, ZA</td>
<td></td>
</tr>
<tr>
<td>Glucocorticoid</td>
<td>≥ 7.5 mg/d</td>
<td>≥ 7.5 mg/d</td>
<td>≥ 5 mg/d ≤ 1 mo or any dose &gt; 1 mo</td>
</tr>
<tr>
<td>Alen, Ris, ZA</td>
<td>Alen, Ris, ZA</td>
<td>Alen, Ris, ZA, Teri</td>
<td></td>
</tr>
</tbody>
</table>

Arthritis Care Res 10:62:1515-26

Physiology – Bone Remodeling


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**Bone Resorption**

Steps, Signals, and Pharmacology

**Osteoporosis and Other Bone Disorders. in Pharmacotherapy:** A Pathophysiologic Approach, 9th ed. DiPiro et al, eds. The McGraw-Hill Co., Inc.

**Bone Formation**

Steps, Signals, and Pharmacology

**Osteoporosis and Other Bone Disorders. in Pharmacotherapy:** A Pathophysiologic Approach, 9th ed. DiPiro et al, eds. The McGraw-Hill Co., Inc.

**Abbreviations**

**Osteoporosis and Other Bone Disorders. in Pharmacotherapy:** A Pathophysiologic Approach, 9th ed. DiPiro et al, eds. The McGraw-Hill Co., Inc.

**Bisphosphonates – Products and Doses**

**Osteoporosis and Other Bone Disorders. in Pharmacotherapy:** A Pathophysiologic Approach, 9th ed. DiPiro et al, eds. The McGraw-Hill Co., Inc.

**Bisphosphonates**

Advantages

- Use since 1995
- Multiple indications
- Women, men, GIO, secondary
- Good evidence
- Hip, spine and non-vertebral fracture prevention
- Oral and injectable agents
- Only liquid formulation
- Weekly or monthly use for oral
- Generic and brand agents
- Few common ADRs
- Prevent some chemotherapy induced bone loss (zoledronic acid)

Disadvantages

- Antiresorptive MOA
- Long duration in bone/body
- Complicated administration
- Suboptimal adherence
- Limited use with decreased renal function
- Expensive injectable
- Serious ADRs with long term use
- Atypical fractures
- Osteonecrosis of the jaw
- Drug holiday

**Antiresporption and Formation Medications**

**Osteoporosis and Other Bone Disorders. in Pharmacotherapy:** A Pathophysiologic Approach, 9th ed. DiPiro et al, eds. The McGraw-Hill Co., Inc.

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### RANKL Inhibitors

**Advantages**
- Good evidence
- Hip, nonvertebral, and spine fracture prevention
- Twice year administration
- Few common side effects
- No renal elimination
- Prevent some chemotherapy induced bone loss

**Disadvantages**
- Serum calcium before administration
- Health care provider administration
  - Rubber allergy
  - Expensive
  - Patient assistance program
  - Prior authorization
  - REMS
  - Refrigeration of product
  - Serious ADRs with long-term use
    - Few cases osteonecrosis of the jaw

### Estrogen Agonist/Antagonist

**Advantages**
- Good evidence
- Spine fracture prevention
- Breast cancer prevention

**Disadvantages**
- No hip fracture prevention
- Hot flushes and clots
- Box warning for fatal stroke

### Tissue Selective Estrogen Complex

**Advantages**
- Some BMD evidence
- Menopausal symptom relief

**Disadvantages**
- Antiresorptive agent
- No fracture evidence
- Less effective than estrogen alone for bone
- ADR profile of raloxifene and estrogens
  - WHI data and concerns

### Calcitonin

**Advantages**
- Some evidence
- Spine fracture prevention
- Modest analgesic effect

**Disadvantages**
- Antiresorption agent
- No hip fracture prevention
- FDA did not find sufficient evidence for cancer risk
- High discontinuation rate
- Patient dislike of a nasal product

### Teriparatide

**Advantages**
- Formation agent
- Good evidence
- Spine and non-vertebral fracture prevention
- FDA approval for women, men, and GIO
  - High risk patients

**Disadvantages**
- No hip fracture prevention
- 2 year limit
- Expensive
- Prior authorization
- Daily injectable agent
- Need normal calcium conc
- Box warning osteosarcoma

### New Formation Medication Classes
**Bone Formation**

- **Steps, Signals, and Pharmacology**
  - **Parathyroid Hormone Receptor Type 1 Peptide (PTHrP) Analog**
    - Abaloparatide – synthetic analog of PTHrP (1-34)
      - Formation medication
      - More RG vs. RO ligand binding with teriparatide
      - Differences in conformations of the PTH receptor
      - Differences in signaling pathway effects
      - Greater formation > resorption effects
    - Radius Health, Inc.
    - Dose – 80 mcg sc daily
    - PDUFA date = March 30, 2017

**Abaloparatide – Fracture Prevention**

- **ACTIVE trial - international study (28 centers, 10 countries)**
- Participants = 2463 (74% completion), mean age 69 yo
  - Postmenopausal women 49-86 yo with osteoporosis
  - Women > 65 yo with osteoporosis
  - T-score -2.5 to -5.0 and atraumatic spine fracture OR
  - Women > 65 yo with osteoporosis
  - T-score -3.0 to -5.0 or fracture with T-score ≤ -2.0
  - Off osteoporosis prescription medications for 5 yrs for bisphosphonates
  - 1 yr for denosumab
- Intervention – placebo, blinded abaloparatide, or open-label teriparatide for 18 months
- Primary outcome – new morphometric vertebral fractures versus placebo

**ACTIVE Fracture Prevention Results**

- New Morphometric Fractures
- Nonvertebral Fractures

**Abaloparatide BMD Effects**

<table>
<thead>
<tr>
<th>Major Osteoporotic Fracture</th>
<th>Clinical Fractures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abaloparatide</td>
<td>Teriparatide</td>
</tr>
<tr>
<td>Sig vs. Placebo and RX</td>
<td></td>
</tr>
</tbody>
</table>

**ACTIVE trial (18 mo)**

- **Similar increases in bone formation markers to teriparatide**
- **Lower increases in bone resorption markers to teriparatide**
- **Potentially less resorption effects**
- **Subset analyzes showed similar BMD changes across various baseline risk factors**

*J Bone Min Res 16; 31 online*
**Abaloparatide to Alendronate Fracture Data**

- New Morphometric Vertebral Fracture
- Major Osteoporotic Fracture

**ACTIVE and ACTIVExtend BMD**

- Femoral Neck
- Lumbar Spine

Abaloparatide ADRs

- Similar profile to placebo and teriparatide
- Significantly less hypercalcemia (3.4%) than teriparatide (6.4%) but more than placebo (0.4%)
- ADRs 10% - 17%
  - Hypercalciuria, dizziness, orthostatic hypertension
- ADRs 5% – 9.9%
  - Arthralgia, back pain, N, URI, HA, HTN, flu, nasopharyngitis, UTI, palpitations

Abaloparatide

- Advantages
  - Formation agent
  - Pivotal evidence with comparison data
  - Potential edge over teriparatide
  - Some sequential data
  - Spine and nonvertebral fracture prevention
  - ADRs similar to placebo and teriparatide, however less hypercalcemia than teriparatide

- Disadvantages
  - No hip fracture trial
  - Unknown cost
  - ? prior authorization
  - Daily sc injection
  - Rat data - osteosarcoma

**Bone Formation Steps, Signals, and Pharmacology**

- Mesenchymal cell
- Osteoblast Differentiation
- Bone Formation Inhibition

**Anti-Sclerostin Agents**

- Romosozumab - Evenity™
  - Formation agent
  - Monoclonal antibody that binds and inhibits sclerostin from inhibiting osteoblasts
- Amgen Inc and UCB Pharmaceuticals
- Dose – 120 mg sc monthly
- PDUFA – July 17, 2017
Romosozumab to Denosumab
Sequential Therapy Fracture Prevention

- FRAME trial - international study - 26 countries
- Participants = 7180 (completion 89% 1 yr, 84% 2 yr)
  - Postmenopausal women 55-90 yo with osteoporosis T-score -2.5 to -3.5 for total hip or femoral neck
  - Mean age 71 yo
  - Corrected 25(OH) vitamin D then calcium 500 – 1000 mg and vitamin D 600 – 800 units
  - Excluded if hip fracture or more than 2 moderate vertebral fractures
- Intervention – romosozumab 210 mg sc injection monthly for 1 yr followed by denosumab 60 mg every 6 mo for 1 yr
- Primary outcome – new vertebral fractures at 12 and 24 mo

Cosman, et al. NEJM 16;375:1532-43

FRAME Fracture Prevention Results

<table>
<thead>
<tr>
<th>Year 1</th>
<th>Year 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Vertebral Fractures</td>
<td>P &lt; 0.001; RR 0.27</td>
</tr>
<tr>
<td>Nonvertebral Fractures</td>
<td>P &lt; 0.001; RR 0.25</td>
</tr>
<tr>
<td>Clinical Fractures</td>
<td></td>
</tr>
</tbody>
</table>

Percen

FRM Fracture Prevention Results

<table>
<thead>
<tr>
<th>Nonvertebral Fractures</th>
<th>Clinical Fractures</th>
</tr>
</thead>
<tbody>
<tr>
<td>P = 0.10 HR = 0.75</td>
<td>P = 0.008 HR = 0.64</td>
</tr>
</tbody>
</table>

FRM BMD Data

<table>
<thead>
<tr>
<th>FMO</th>
<th>Romosozumab</th>
<th>Placebo</th>
<th>Alendronate</th>
<th>Teriparatide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>N=50</td>
<td>N=50</td>
<td>N=51</td>
<td>N=49</td>
</tr>
<tr>
<td>BMD Changes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Hip</td>
<td>4.1%</td>
<td>-0.7%</td>
<td>4.9%</td>
<td>1.3%</td>
</tr>
<tr>
<td>Femoral Neck</td>
<td>3.7%</td>
<td>-1.1%</td>
<td>1.2%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Lumbar Spine</td>
<td>11.3%</td>
<td>0.0%</td>
<td>4.1%</td>
<td>7.1%</td>
</tr>
</tbody>
</table>

FRM BMD Effects

<table>
<thead>
<tr>
<th>Year 1</th>
<th>Year 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Hip</td>
<td>6.8%</td>
</tr>
<tr>
<td>Femoral Neck</td>
<td>5.2%</td>
</tr>
<tr>
<td>Lumbar Spine</td>
<td>13.3%</td>
</tr>
</tbody>
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FRM Abstracts

- 436 postmenopausal women – STRUCTURE
  - Prior alendronate therapy with T-score ≤ -2.5 and fracture

1 year

- Total hip | 2.9% | -0.5% (Sig) |
- Lumbar spine | 0.8% | 5.4% (Sig) |

- 245 men phase 3 one year trial – BRIDGE
  - Osteoporosis or osteoporotic fracture
  - BMD changes from baseline, which were significant from placebo:
    - Total hip 2.5%
    - Femoral neck 2.2%
    - Lumbar spine 12.1%
  - ACR/ARHP Annual Meeting November 2016, Wash DC
Romosozumab ADRs

- Similar profile to placebo
- Serious ADRs 9.6% vs. placebo 8.7%
  - 2 cases ONJ
  - 1 case atypical fracture
- ADRs 10.5% - 13%
  - Arthralgia, nasopharyngitis, back pain
- ADRs 5% – 9.9%
  - Osteoarthritis, hypersensitivity, injection site reaction
- Binding anti-romosozumab antibodies – 18%
- Neutralizing antibodies – 0.7%
  
  NEJM 16;375:1532-43

Romosozumab

**Advantages**
- Formation agent
- Pivotal trial evidence with comparison data
  - Greater BMD changes than alendronate and teriparatide
  - Sequential data
- Spine and nonvertebral fracture prevention
- Sequential therapy and men BMD data
- Once monthly administration
- ADRs similar to placebo

**Disadvantages**
- No hip fracture data
- Unknown cost
- ? prior authorization
- Few cases of ONJ and atypical fractures

Conclusion

- Guidelines encourage sequential therapy beginning with a formation medication.
- Abaloparatide increases bone formation by increasing osteoblasts and their functioning.
- Romosozumab increases bone formation by preventing sclerostin from inhibiting osteoblast action.
- Abaloparatide and romosozumab prevent vertebral and clinical fractures in postmenopausal women.
- Abaloparatide and romosozumab produce greater BMD effects than teriparatide.
- Antiresorptive therapy after abaloparatide increases BMD further.
- Romosozumab increases BMD before and after antiresorptive therapy and in men.

Case Discussion

- Ms. Johnson  Chronic kidney disease
- Mr. Runninghorse  Very low BMD
  Secondary osteoporosis
- Ms. Martindale  Osteoporosis fracture while on an antiresorptive medication

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