Challenges in the Management of Osteoporosis and Vitamin D Deficiency in the HIV-infected Patient

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Why worry about osteoporosis?

- Osteoporosis is common among older populations
- Osteoprotic fractures are a major source of morbidity & mortality
- Osteoporosis is a silent disease until fractures occur
- Osteoporosis can be detected in a pre-clinical stage and fractures can be prevented
Prevalence of Osteoporosis in HIV-infected Patients vs HIV-uninfected Controls: A Meta-analysis

Overall prevalence of osteoporosis in HIV-infected patients  15%

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiel (2004)</td>
<td>5.03 (1.47, 17.27)</td>
</tr>
<tr>
<td>Brown (2004)</td>
<td>4.26 (0.22, 82.64)</td>
</tr>
<tr>
<td>Bruera (2003)</td>
<td>4.51 (0.26, 79.27)</td>
</tr>
<tr>
<td>Dolan (2004)</td>
<td>2.11 (0.54, 8.28)</td>
</tr>
<tr>
<td>Huang (2002)</td>
<td>3.52 (0.15, 81.92)</td>
</tr>
<tr>
<td>Knobel (2001)</td>
<td>5.13 (1.80, 14.60)</td>
</tr>
<tr>
<td>Loiseau-Peres (2002)</td>
<td>4.28 (0.46, 39.81)</td>
</tr>
<tr>
<td>Madeddu (2004)</td>
<td>29.84 (1.80, 494.92)</td>
</tr>
<tr>
<td>Tebas (2000)</td>
<td>3.40 (0.19, 61.67)</td>
</tr>
<tr>
<td>Teichman (2003)</td>
<td>17.41 (0.97, 313.73)</td>
</tr>
<tr>
<td>Yin (2005)</td>
<td>2.37 (1.09, 5.16)</td>
</tr>
<tr>
<td>Overall (95% CI)</td>
<td>3.68 (2.31, 5.84)</td>
</tr>
</tbody>
</table>

Brown, AIDS, 2006

8,525 HIV-infected
2,208,792 non HIV-infected patients

Tiant, JCEM, 2008
Definitions

Osteoporosis:
“systemic skeletal disorder characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and fracture”
Vertebral body: Normal vs Osteoporosis

normal

osteoporotic
Definitions

Functional Definition (DXA)- WHO Definition

- Osteoporosis: T-score < -2.5
- Osteopenia: T-score = -1.0 to -2.5
- Normal: T-score > -1.0

↑ Risk of fracture by 1.5-3.0 x for each SD decrease

Caveats:

- Z-score (<-2.0) used in men < 50 years and premenopausal women
- BMD explains only about 50% of fracture risk
Pathophysiology and Risk Factors

- HIV Disease Factors
  - Inflammation and Viral Proteins
    - \( \uparrow \) bone resorption
    - \( \downarrow \) bone formation
- Medication Factors
  - Tenofovir
  - Certain PIs (ATV/r)
  - ART initiation (\( \downarrow 2-6\% \) over 96 weeks)
## Randomized, Controlled Trials Comparing BMD in TDF vs Non-TDF Regimens

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>duration (wks)</th>
<th>Non-TDF</th>
<th>Sites</th>
<th>TDF Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gallant, 2004</td>
<td>602</td>
<td>144</td>
<td>d4T</td>
<td>Hip, Spine</td>
<td>Spine :-2.2% v -1.0% Hip : :-2.8% v -2.4%</td>
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<tr>
<td>Moyle, 2009</td>
<td>385</td>
<td>48</td>
<td>ABC</td>
<td>Hip, Spine</td>
<td>Spine: -2.4% v -1.6% Hip: -3.6% v -1.9%</td>
</tr>
<tr>
<td>McComsey, 2010</td>
<td>258</td>
<td>96</td>
<td>ABC</td>
<td>Hip, Spine</td>
<td>Hip: -4.0% v :-2.2% Spine: -3.8%v -1.8%</td>
</tr>
<tr>
<td>Huang, 2010</td>
<td>753</td>
<td>96</td>
<td>AZT, d4T</td>
<td>Total BMD</td>
<td>TDF: -3%; AZT: -1.75%, d4T: -2.0%</td>
</tr>
<tr>
<td>Martin, 2009</td>
<td>352</td>
<td>96</td>
<td>ABC</td>
<td>Hip, Spine</td>
<td>Spine: $\Delta T$ -0.04 v +0.07 Hip: $\Delta T$ -0.07 v +0.09</td>
</tr>
</tbody>
</table>
Antiretroviral Exposure and Risk of Osteoporotic Fractures in VA Study: HAART Era

MV Model 1: Controlling for CKD, age, race, tobacco use, diabetes and BMI;
MV Model 2: Controlling for Model 1 variables + concomitant exposure to other ARVs.

Bedimo, IAS, 2011
Randomized, Controlled Trials Comparing BMD in PI vs Non-PI Regimens

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>duration (wks)</th>
<th>PI</th>
<th>Non-PI</th>
<th>Sites</th>
<th>PI Effect?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tebas, 2007</td>
<td>157</td>
<td>96</td>
<td>NFV</td>
<td>EFV</td>
<td>Total BMC</td>
<td>No</td>
</tr>
<tr>
<td>Bonnet, 2007</td>
<td>74</td>
<td>36</td>
<td>FPV/r, ATV/r</td>
<td>NNRTI</td>
<td>Spine</td>
<td>Total BMD: No Spine: Yes</td>
</tr>
<tr>
<td>Brown, 2009</td>
<td>106</td>
<td>96</td>
<td>LPV/r</td>
<td>EFV</td>
<td>Total BMD</td>
<td>No</td>
</tr>
<tr>
<td>Duvivier, 2009</td>
<td>71</td>
<td>48</td>
<td>LPV/r, IDV/r</td>
<td>EFV, NVP</td>
<td>Hip, Spine</td>
<td>Spine: -4.9% v -1.5% Hip: -2.8% v -2.7%</td>
</tr>
<tr>
<td>McComsey, 2010</td>
<td>258</td>
<td>96</td>
<td>ATV/r</td>
<td>EFV</td>
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<td>EFV</td>
<td>Total BMD</td>
<td>No</td>
</tr>
</tbody>
</table>
## BMD Loss with ART-initiation:
~2-6% at 48-96 weeks

<table>
<thead>
<tr>
<th>Author, y</th>
<th>N</th>
<th>Wks</th>
<th>ART-type</th>
<th>Study outcomes</th>
</tr>
</thead>
</table>
| Gallant, 2004   | 602 | 144 | TDF vs. d4T               | Spine: TDF-2.2%; d4T:-1.0%
|                 |     |     |                           | Hip: TDF: -2.8%; d4T:-2.4%                         |
| Tebas, 2007     | 157 | 96  | NFV vs EFV                | 2.5% decrease in total BMC                          |
| Bonnet, 2007    | 74  | 36  | PI vs non-PI              | 0.8% decrease in lumbar BMD                         |
| Brown, 2009     | 106 | 96  | LPV/r vs AZT/3TC/EFV      | 2.5% loss in total BMD                             |
| Duvivier, 2009  | 71  | 48  | PI vs Non-PI              | Spine: -4.1%, Hip: -2.8%                           |
| van Vonderen, 2009 | 50  | 104 | AZT/3TC/LPV/r v NVP/LPV/r | Fem Neck: -6.3% v -2.3%                             |
|                 |     |     |                           | Spine: -5.1 v -2.6%                                 |
| Moyle, 2009     | 385 | 48  | TDF v ABC                 | Hip: ABC:-1.9%; TDF: -3.6%
|                 |     |     |                           | Spine:ABC:-1.6%; TDF: -2.4%                        |
| McComsey, 2010  | 258 | 96  | TDF v ABC                 | Hip: ABC:-2.2%; TDF: -4.0%
|                 |     |     | ATV/r vs EFV              | Spine:ABC: -1.8%; TDF: -3.8%
|                 |     |     |                           | Hip: ATV/r:-3.5%; EFV: -3.5%
|                 |     |     |                           | Spine:ATV/r:-3.0%; EFV: -2.0%                      |
| Huang, 2010     | 753 | 96  | TDF v AZT v d4T           | Total BMD: TDF: -3%; v AZT: -1.75% v d4T: -2%
|                 |     |     | LPV/r vs EFV              | Difference LPV/r vs EFV: -0.5%                     |
| Qaqish, 2011    | 160 | 96  | LPV/r+RAL v LPV/r+TDF/FTC | Total BMD: +0.68 v -2.5%                            |
| Tebas, 2011     | 349 | 96  | RPV vs EFV (+NRTI)        | Total BMD: -1.5% vs -1.5%                          |
| Moyle, 2011     | 224 | 96  | ATV/r v LPV/r (+TDF/FTC)  | Total BMD: -3% v -4%                               |
Average 2-year Percent Change in BMD in Healthy Women

Warming, Osteo Int, 2002
Bone Loss in Patients Initiating Glucocorticoid Treatment

• 120 patients initiating GCs (≥7.5 mg/day of prednisone or equivalent)

• All patients received 500 mg calcium/day

• ↓ 3%/year at all sites in placebo group
Pathophysiology and Risk Factors

• Patient-Related Factors
  – Low Body Weight
  – Smoking
  – Alcohol Use
  – Opiate Use
  – Hepatitis C Co-infection
  – Physical Inactivity
  – Hypogonadism
  – Low Vitamin D
To Screen or Not to Screen….
2008 US National Osteoporosis Foundation (NOF) Guidelines for DXA Screening

- Those with a history of fragility fracture
- Women $\geq 65$ yrs, Men $\geq 70$
- Postmenopausal women and men 50-70 years, if there is concern based on risk factor profile (HIV and/or HAART not listed among risk factors)
“we recommend a DXA scan for all HIV-infected post-menopausal women and men >50 years”
Recomendações para avaliação de densidade óssea

1.1. Mulheres com idade igual ou superior a 65 anos e Homens com idade igual ou superior a 70 anos.
1.2. Mulheres na pós-menopausa, ainda que abaixo de 65 anos, e homens entre 50 e 70 anos de idade, com fatores de risco.
1.3. Homens com idade inferior a 70 anos e com fatores de risco para fraturas.
1.4. Adultos com história de fratura por fragilidade, doença ou condição ou medicamentos associados à baixa massa óssea ou perda óssea.
1.5. Pessoas para as quais são consideradas intervenções farmacológicas para osteoporose.
1.6. Indivíduos em tratamento para osteoporose, para monitorar a eficácia do tratamento.
1.7. Pessoas que não estejam realizando tratamento, nas quais a identificação de perda de massa óssea possa determinar a indicação do tratamento.
1.8. Mulheres com idade entre 40 e 50 anos - período de transição menopausal - com fatores de risco para fraturas

II Reunião de Desenvolvimento das Posições Oficiais SBDens
14 de Outubro de 2008
2008 US NOF Guidelines: Who to Treat*

- Those with hip or vertebral fractures
- Those with BMD T-scores $\leq -2.5$ at the femoral neck, total hip, or spine by DXA
- Those with T-score b/t -1 and -2.5 (osteopenia) at above sites AND 10-year hip fracture probability $\geq 3\%$ or 10-year all major osteoporosis-related fracture $\geq 20\%$ based on FRAX model

*applies to post-menopausal women and men $\geq 50$ years
Calculation Tool

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

**Questionnaire:**

1. Age (between 40-90 years) or Date of birth
   - Age: 
   - Y: 
   - M: 
   - D: 
2. Sex  
   - Male  
   - Female
3. Weight (kg)
4. Height (cm)
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 more units per day  
   - No  
   - Yes
12. Femoral neck BMD  
   - Select

**Risk factors**

For the clinical risk factors a yes or no response is asked for. If the field is left blank, then a "no" response is

http://www.shef.ac.uk/FRAX/
Case Presentation: AD

- 62 year old white male referred to LD clinic for body fat changes
- HIV dx’d 1987, nadir CD4 22, from 1997 to 2002 on d4T/3Tc/IDV, currently ABC/AZT/3Tc/EFV
- H/O hypogonadism on transdermal T
- H/O COPD (60 pk-yr tobacco hx), multiple steroid courses
- No h/o fracture, no height loss
Case Presentation: AD

Dual X-ray Absorptiometry

<table>
<thead>
<tr>
<th></th>
<th>T-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1-L4</td>
<td>-2.2</td>
</tr>
<tr>
<td>Femoral Neck</td>
<td>-2.1</td>
</tr>
<tr>
<td>Total Hip</td>
<td>-2.3</td>
</tr>
</tbody>
</table>
Questionnaire:

1. Age (between 40-90 years) or Date of birth
   - Age: 63
   - Date of birth: Y: [ ], M: [ ], D: [ ]

2. Sex
   - [ ] Male
   - [ ] Female

3. Weight (kg) 65.77

4. Height (cm) 175.3

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 more units per day
    - [ ] No
    - [ ] Yes

12. Femoral neck BMD
    - T-score: -2.3
    - Clear
    - Calculate

BMI 21.4

The ten year probability of fracture (%) with BMD:

- Major osteoporotic: 18
- Hip fracture: 4.10
“It is not recommended to use any of the populations available in the FRAX tool, as a substitute for the Brazilian population”

Pinheiro, Arq Bras Endocrinol Metab. 2009;53(6):783-90
Who to treat?: Brazilian Guidelines

- Those with vertebral and/or hip fracture.
- Those with BMD T-scores ≤ -2.5 at the lumbar spine, femoral neck and total hip.
- Postmenopausal women and men aged 50 years and older who have lower bone mass (T-score between -2.5 to -1.0) at femoral neck, total hip and lumbar spine if in addition have other fracture risk factors.

Courtesy of Dr. Francisco Jose Albuquerque de Paula, University of São Paulo, Ribeirão Preto
Secondary Causes of Low BMD

- Vitamin D deficiency → 25 OH Vit D
- Hyperparathyroidism → PTH, Ca++
- Subclinical Hyperthyroidism → TSH
- Hypogonadism → Males: Free Testosterone
- Phosphate wasting → Fractional Excretion of Phosphate
- Idiopathic Hypercalciuria → 24 hr Urinary Calcium
- Celiac Sprue → Tissue Transglutaminase
- Multiple Myeloma → Serum Protein Electrophoresis
- Mastocytosis → Serum Tryptase
- Cushing’s Syndrome → 24 hr Urinary Free Cortisol
Secondary Causes of Low BMD

- Vitamin D deficiency $\rightarrow$ 25 OH Vit D
- Phosphate wasting $\rightarrow$ Fractional Excretion of Phosphate
Osteomalacia

• Impaired bone mineralization
• Accompanied by weakness, fracture, pain, anorexia, and weight loss
• Treated with Vitamin D, Ca++, +/- phosphate, not bisphosphonates
• Most important differential diagnosis for low BMD
RB

- 51 y/o WM with HIV dx’d in 2001, nadir CD4 30, VL< 50 on TDF/FTC/EFV, but CD4 cell count 150-250
- Drinks 3-4 glasses wine/day, former smoker
- Sister with osteoporosis, no fx
- H/O two traumatic fractures (boating and glade skiing)
Case Presentation: RB

Dual X-ray Absorptiometry

<table>
<thead>
<tr>
<th></th>
<th>T-score</th>
<th>Z-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1-L4</td>
<td>-2.9</td>
<td>-2.5</td>
</tr>
<tr>
<td>Femoral Neck</td>
<td>-1.4</td>
<td>-0.6</td>
</tr>
<tr>
<td>Total Hip</td>
<td>-0.8</td>
<td>-0.4</td>
</tr>
</tbody>
</table>

FRAX (femoral neck): 10 y all osteoporotic fx 4.7%/hip fx 0.5%
Secondary work-up:

- 25 OH Vit D 15 ng/mL (37 mmol/L)
- PTH 44 pg/ml
- Ca++ 9.5 mg/dL
- TSH 1.8 mU/L
- Free Testosterone 61 pg/ml
- Serum Phosphate 3.0 mg/dl
- Fractional Excretion Phos 10%
Definitions of Vitamin D Status

- "deficiency"
- "inadequacy"
- "normal"

25 mmol/L, 50, 75

Change in 25OHD with ART-initiation: EFV vs non-EFV

Adjusted* Mean Difference(SEM): -5.1 ± 1.5 ng/mL, p=0.001

-12.8 mmol/L

*Adjusted for baseline 25(OH)D, race, season

Brown, Antiviral Therapy, 2010
Vitamin D metabolism

SKIN

7-dehydrocholesterol

SKIN

previtamin D₃

SKIN

vitamin D₃

25 hydroxylase

LIVER

24 hydroxylase

TARGET ISSUES

Calcitriol

1α hydroxylase

KIDNEY

1, 25-dihydroxyvitamin D₃

25-hydroxyvitamin D₃
Vitamin D metabolism

EFV

↓

24,25 dihydroxyvitamin D

Calcitroic Acid

24 hydroxylase

TARGET ISSUES

1 α hydroxylase

KIDNEY

1, 25 – dihydroxyvitamin D₃

24 hydroxylase (CYP24A)

25 – hydroxyvitamin D₃
Treatment of Vitamin D Deficiency

Replacement

• Ergocalciferol (D$_2$) 50K units 1-2 times/week for 8-12 weeks

OR

• Cholecalciferol (D$_3$) 2000 IU/d

Maintenance

• Ergocalciferol 50K units 1-2 times/month

OR

• Cholecalciferol 1000-2000 IU/d

Rule of Thumb: 100 IU D3/d will increase 25 OH D by 1 ng/mL
Management: RB

- Plain films of thoracic and lumbar spine
- Vitamin D replacement
  - D2 50K q week x 12 weeks
  - 2000 IU D3 daily
- Ca++ 1000 mg
- Continue exercise
2/3 of those with subclinical vertebral fractures did not have osteoporosis.
To Screen or Not to Screen....
IOM Recommendations in General Population: 2010

- No screening recommendations
- Universal supplementation
  - Adults < 70 yrs: 600 IU/d
  - Adults > 70: 800 IU/d
1.1. We recommend screening for vitamin D deficiency in individuals at risk for deficiency. We do not recommend population screening for vitamin D deficiency in individuals who are not at risk (1 | ☒ ☒ ☒ ☒ ☒).
<table>
<thead>
<tr>
<th>TABLE 2. Indications for 25(OH)D measurement (candidates for screening)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rickets</td>
</tr>
<tr>
<td>Osteomalacia</td>
</tr>
<tr>
<td>Osteoporosis</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
</tr>
<tr>
<td>Hepatic failure</td>
</tr>
<tr>
<td>Malabsorption syndromes</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
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<tr>
<td>Inflammatory bowel disease</td>
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<tr>
<td>Crohn’s disease</td>
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<tr>
<td>Bariatric surgery</td>
</tr>
<tr>
<td>Radiation enteritis</td>
</tr>
<tr>
<td>Hyperparathyroidism</td>
</tr>
<tr>
<td>Medications</td>
</tr>
<tr>
<td>Antiseizure medications</td>
</tr>
<tr>
<td>Glucocorticoids</td>
</tr>
<tr>
<td>AIDS medications</td>
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<tr>
<td>Antifungals, e.g. ketoconazole</td>
</tr>
<tr>
<td>Cholestyramine</td>
</tr>
<tr>
<td>African-American and Hispanic children and adults</td>
</tr>
<tr>
<td>Pregnant and lactating women</td>
</tr>
<tr>
<td>Older adults with history of falls</td>
</tr>
<tr>
<td>Older adults with history of nontraumatic fractures</td>
</tr>
<tr>
<td>Obese children and adults (BMI 30 kg/m²)</td>
</tr>
<tr>
<td>Granuloma-forming disorders</td>
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<tr>
<td>Sarcoidosis</td>
</tr>
<tr>
<td>Tuberculosis</td>
</tr>
<tr>
<td>Histoplasmosis</td>
</tr>
<tr>
<td>Coccidiomycosis</td>
</tr>
<tr>
<td>Berylliosis</td>
</tr>
<tr>
<td>Some lymphomas</td>
</tr>
</tbody>
</table>
Concerns Regarding Universal Screening

- Benefit of vitamin D replacement not clear for conditions except for fracture and falls
- Measuring 25OHD is not cheap ($57 at Quest)
- The best way to increase 25OHD into the target range is not clear and some approaches may be associated with harm
Does it matter how 25OHD is increased into the target range?: A Recent Randomized Trial

- 2256 women ≥ 70 years
- Randomized to 500,000 IU D3 orally each fall
- Followed 3-5 years

Sanders, JAMA, 2010
Annual high dose vitamin D associated with increased falls and fractures

Sanders, JAMA, 2010
Treatment of Vitamin D Deficiency

Replacement
Ergocalciferol (D$_2$)
50K units 1-2 times/week for 8-12 weeks
OR
• Cholecalciferol (D$_3$) 2000 IU/d

Maintenance
• Ergocalciferol
50K units 1-2 times/month
OR
• Cholecalciferol
1000-2000 IU/d

Rule of Thumb: 100 IU D3/d will increase 25 OH D by 1 ng/mL
Dealing with Vitamin D: My Strategy

• No universal screening
• If BMD is normal and no falls, no need to check 25OHD
  – Universal replacement with 1000 IU/d D3
  – If taking EFV, consider 2000 IU/d
Dealing with Vitamin D: My Strategy

- If BMD is low or history of falls, check 25OHD:
  - >30 ng/mL (75 mmol/L): 1000 IU/d
  - 20-30 ng/mL (50-75 mmol/L): 2000 IU/d
  - 15-20 ng/mL (37.5-50 mmol/L): Ergocalciferol 50K units weekly x 8 weeks, then D3 2000 IU/d
  - <15 ng/mL (37.4 mmol/L): Ergocalciferol 50K units once or twice a week x 8-12 weeks, then D3 2000 IU/d, recheck 25OHD after ergo course

- More aggressive replacement if PTH is high or s/s of osteomalacia
RB: new

- 71 y/o WM with HIV dx’d in 2001, nadir CD4 30, VL< 50 on TDF/FTC/EFV, but CD4 cell count 150-250
- Drinks 3-4 glasses wine/day, former smoker
- Sister with osteoporosis, no fx
- H/O two traumatic fractures (boating and glade skiing)
Management Options

• General recommendations
  – Calcium/vitamin D supplementation
  – Smoking cessation, Alcohol reduction
  – Weight-bearing exercise
  – Assess fall risk (Are you worried about falling?)
    • Strength/Balance Training

• ? Switch ART (off TDF, on RAL)

• Pharmacologic Treatment
### Table 2: Bone Mineral Density at 24 and 48 Weeks

<table>
<thead>
<tr>
<th></th>
<th>Mean % Change from Baseline [95% CI]</th>
<th>Week 24</th>
<th>P</th>
<th>Week 48</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spine</td>
<td>1.5 [0.5, 2.5]</td>
<td>0.0038</td>
<td>3.0 [1.9, 4.0]</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Left hip</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total hip</td>
<td>1.4 [0.8, 2.0]</td>
<td>0.0001</td>
<td>2.5 [1.6, 3.3]</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Femoral neck</td>
<td>1.5 [0.3, 2.7]</td>
<td>0.0131</td>
<td>2.1 [0.9, 3.2]</td>
<td>0.0011</td>
<td></td>
</tr>
<tr>
<td>Right hip</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total hip</td>
<td>0.6 [−0.3, 1.5]</td>
<td>0.1902</td>
<td>2.7 [1.9, 3.5]</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>
Management Options

• General recommendations
• ? Switch ART
• Pharmacologic Treatment
  – Bisphosphonates
  – Selective estrogen receptor modulator
  – Estrogen
  – PTH analogue
  – Denosumab
  – Strontium Ranelate
Considerations When Choosing Between Bisphosphonates

<table>
<thead>
<tr>
<th></th>
<th>Alendronate</th>
<th>Risedronate</th>
<th>Ibandronate</th>
<th>Zoledronate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Efficacy</strong></td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td><strong>Cost (1 year)</strong></td>
<td>$350</td>
<td>$1200</td>
<td>$1200</td>
<td>$1100</td>
</tr>
<tr>
<td><strong>Compliance</strong></td>
<td>-</td>
<td>-</td>
<td>- (oral)/ + (IV)</td>
<td>+</td>
</tr>
<tr>
<td><strong>GI Side Effects</strong></td>
<td>Yes (20%)</td>
<td>Yes (20%)</td>
<td>Yes (oral)/No(IV)</td>
<td>No</td>
</tr>
<tr>
<td><strong>Osteonecrosis of the Jaw</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Acute Phase Reaction</strong></td>
<td>No</td>
<td>No</td>
<td>No (oral)/Yes(IV)</td>
<td>Yes (~10%)</td>
</tr>
<tr>
<td><strong>Atrial Fibrillation</strong></td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td><strong>Esophageal Cancer</strong></td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>No</td>
</tr>
<tr>
<td><strong>Atypical Femur Fracture</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Conclusions

• Fractures likely to be a major source of morbidity for aging HIV-infected patients
• Etiology is multifactorial
• Some HIV medications have direct effects on bone (Tenofovir and PIs) and vitamin D (Efavirenz)
• HIV treatment initiation is associated with bone loss
• Non-skeletal risk factors for fracture deserve further investigation
• DXA screening recommended in HIV-infected patients ≥ 50 yrs
• Screening for secondary causes is critical, especially for phosphate wasting in those on tenofovir
• Treatment guidelines should follow those established for the general population