Cases from the HIV Endocrine/Metabolic Clinic

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Faculty and Planning Committee Disclosures
Please consult your program book or the Conference App.

Off-Label Disclosure
There will discussion of off-label uses of approved agents.
Learning Objective

• Implement optimal evaluation and management strategies of endocrine and metabolic diseases in the care of people living with HIV

Endocrine and Metabolic Diseases are More Common Among HIV-infected Persons

• Diabetes Mellitus
• Dyslipidemia
• Hypogonadism
• Body Composition Changes
• Osteoporosis
Important Role of Inflammation

- Diabetes Mellitus
- Dyslipidemia
- Hypogonadism
- Body Composition Changes
- Osteoporosis

Causes of Endocrine and Metabolic Diseases in HIV

- Patient Factors
- Medication
- Disease
Case 1

- 60 y/o AAM with HCV, HIV on ART; TDF/FTC/DRV/r (CD4 369, VL<50)
- Referred for consideration of re-initiation T therapy
- In 2011, 6 lb weight loss
- No weakness, fatigue.
- Some erectile dysfunction, loss of libido
- Started transdermal testosterone
- No change in weight, no change in sexual function

Case 1

- Skin rash with transdermal preparations
- PSA 2→4.5, biopsy negative
- No change in sexual symptoms on T.
- No change in constitutional symptoms on T.
- Stopped T. No change in any symptoms
Case 1

- Does he have signs/symptoms of low T?
  - +ED, slight ↓ libido
  - BMI 19 (no recent change in muscle mass)

Signs and Symptoms by Specificity

**More Specific**
- ↓ libido
- ↓ spontaneous erections
- gynecomastia
- ↓ body hair
- Small testes
- infertility
- ↓ bone density, fracture
- hot flushes

**Less Specific**
- ↓ energy, motivation, confidence
- depressed mood
- ↓ concentration/memory
- sleep disturbance
- anemia
- ↓ muscle bulk and strength
- ↑ body fat
- ↓ work performance

Bhasin, JCEM, 2010
Case 1

• Does he have signs/symptoms of low T?
  – +ED, slight ↓ libido
  – BMI 19 (no recent change in muscle mass)
• Does he have biochemical evidence of low T?
  – Total T 422 ng/dL (nl >300)

Regulation of Testosterone

FT = free testosterone; SHBG = sex-hormone binding globulin.

Adapted from Braunstein GD. Basic & Clinical Endocrinology. 5th ed. Stamford, Conn. Appleton & Lange; 1997:422-452.
Age-Adjusted Sex Hormones in Men by HIV-Status

Proportion of hypogonadal men with Normal T, Low FT by HIV Status
Diagnosis of Androgen Deficiency in HIV-infected Men

Symptoms consistent with androgen deficiency with no other obvious explanation.

Obtain free AM testosterone levels.

Start with morning free testosterone given possible SHBG abnormalities


Case 1

• Does he have signs/symptoms of low T?
  – +ED, slight ↓ libido
  – BMI 19 (no recent change in muscle mass)

• Does he have biochemical evidence of low T?
  – Total T 422 (nl >300)
  – FT 17 (nl 46-224)
  – LH 18 (1.7, 11.2), FSH 35.7 (1.5, 12.4)
To Treat or Not To Treat? : Weighing Risks and Benefits

Potential Benefits of Testosterone Therapy in Older Men

Bhasin S et al. J Clin Endocrinol Metab. 2010;95:2536
Case 1

- What are the potential benefits of treatment?
  - ? Improvement in sexual function

Relationship of Serum Testosterone to Erectile Function

Rhoden, J Urology 167:1748, 2002
Relationship of Serum Testosterone to Sexual Symptoms

Wu, NEJM, 2010

Effect of T on Sexual Function: T Trials

Snyder, Endocrine Rev, 2018
Case 1

• What are the potential benefits of treatment?
  – ? Improvement in sexual function
  – ? Improvement in fatigue
  – ? Maintain lean mass
  – ? Bone Mineral Density
Effect of Testosterone Treatment on BMD

Snyder, JCEM, 1999

Effect of T on Volumetric BMD: T Trials

Snyder, Endocrine Rev, 2018
Testosterone Use since last visit: BOSS

Grant, AIDS Res Hum Retro, 2018

T use and BMD T-score: Fully Adjusted*

<table>
<thead>
<tr>
<th></th>
<th>Lumbar Spine</th>
<th>Total Hip</th>
<th>Femoral Neck</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV Status (ref: HIV-)</td>
<td>-0.14, p=0.34</td>
<td>-0.23, p=0.03</td>
<td>-0.18, p=0.15</td>
</tr>
<tr>
<td>Age (ref: 50-59 y)</td>
<td>0.4, p=0.006</td>
<td>-0.18, p=0.09</td>
<td>-0.32, p=0.008</td>
</tr>
<tr>
<td>Testosterone Use</td>
<td>0.68, p=0.003</td>
<td>0.17, p=0.30</td>
<td>0.31, p=0.10</td>
</tr>
</tbody>
</table>

*adjusted for race, MACS site, BMI, h/o IDU, EtOH, smoking, physical activity, viral hepatitis, diabetes, depression meds, PPIs, steroid use, FH hip fracture, 25OH vitamin D, free testosterone
T use and BMD T-score: HIV+ with HIV RNA < 50 cp/mL, Fully Adjusted*

<table>
<thead>
<tr>
<th></th>
<th>Lumbar Spine</th>
<th>Total Hip</th>
<th>Femoral Neck</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (ref: 50-59 y)</td>
<td>0.17, p=0.45</td>
<td>-0.31, p=0.05</td>
<td>-0.35, p=0.06</td>
</tr>
<tr>
<td>Testosterone Use</td>
<td>0.95, p=0.002</td>
<td>0.45, p=0.03</td>
<td>0.45, p=0.06</td>
</tr>
</tbody>
</table>

*adjusted for race, MACS site, BMI, h/o IDU, EtOH, smoking, physical activity, viral hepatitis, diabetes, depression meds, PPIs, steroid use, FH hip fracture, 25OH vitamin D, free testosterone, % visits with undetectable VL, CD4, nadir CD4, cumulative HAART, cumulative TDF, cumulative PI, ever thymidine analogue

Case 1

- What are the potential benefits of treatment?
  - ? Improvement in sexual function
  - ? Improvement in fatigue
  - ? Maintain lean mass
  - ? Bone Mineral Density
    - Lumbar Spine T score -2.9
    - Femoral Neck T-score -1.1
    - Total Hip Score T-score -0.7
Case 1

• What are the potential benefits of treatment?
  – ? Improvement in sexual function
  – ? Improvement in fatigue
  – ? Maintain lean mass
  – ? Bone Mineral Density
    • Lumbar Spine T score -2.9
    • Femoral Neck T-score -1.1
    • Total Hip Score T-score -0.7
      – FRAX 10 yr risk: All osteoporotic fx 4.2%; Hip Fx 0.7%
    • No occult vertebral fracture on plain x-ray of spine

Adverse Effects of Testosterone Therapy

Bhasin S et al. J Clin Endocrinol Metab. 2010;95:2536
Increase in Hematocrit with TRT

Snyder, JCEM, 1999

Endocrine Society Guidelines
Erythrocytosis

Against T Therapy

Baseline Hct >50%
(these men should undergo further evaluation)

Monitoring
• Hematocrit at 3 & 6 months—then annually
• Older age and T injections at higher risk

Cessation and Referral

Hct >54%
• Evaluate for hypoxia
• Re-initiate T at lower dose once Hct at safe level

Bhasin S et al., J Clin Endocrinol Metab. 2010;95:2536
Prostate Events in Testosterone Replacement Trials in Middle-aged & Older Men: A Meta-Analysis

<table>
<thead>
<tr>
<th>Event</th>
<th>Rate for Testosterone</th>
<th>Rate for Placebo</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate cancer</td>
<td>5/643</td>
<td>2/427</td>
<td>1.11</td>
<td>0.48, 2.58</td>
</tr>
<tr>
<td>PSA &gt;4 ng/ml</td>
<td>27/643</td>
<td>14/427</td>
<td>1.20</td>
<td>0.68, 2.12</td>
</tr>
<tr>
<td>Prostate Biopsies</td>
<td>21/643</td>
<td>1/427</td>
<td>1.93</td>
<td>0.86, 4.37</td>
</tr>
<tr>
<td>Total prostate events*</td>
<td>56/643</td>
<td>18/427</td>
<td>1.80</td>
<td>1.08, 3.00</td>
</tr>
</tbody>
</table>


Increase in PSA with Testosterone Treatment

Snyder, JCEM, 1999
Endocrine Society Guidelines

Prostate

Against T therapy

- Prostate Cancer
- Nodule
- PSA >4.0 ng/ml
- PSA >3.0 ng/ml (African Americans, Family History)

Monitoring

Men ≥40 yrs with PSA >0.6 ng/ml
PSA at 3 & 6 months—then based on AUA guidelines

Cessation and Referral

- Nodule
- Δ PSA change >1.4 ng/ml
- International Prostate Symptom Score >19

Bhasin S et al. J Clin Endocrinol Metab. 2010;95:2536

CV Events in Testosterone Trials: Shortcomings

- Small sample size
- Short-term follow-up
- Recruited healthy men with normal testosterone levels
- Limited Power to evaluate cardiovascular events
- Lack of structured evaluation and adjudication of cardiovascular adverse events
- Inadequate reporting of adverse events

<table>
<thead>
<tr>
<th>Trials</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copenhagen Study Group, 1986</td>
<td>2.62 (0.01 to ∞)</td>
</tr>
<tr>
<td>English et al., 2000</td>
<td>5.43 (0.19 to ∞)</td>
</tr>
<tr>
<td>Snyder et al., 2001</td>
<td>1.66 (0.46 to 5.91)</td>
</tr>
<tr>
<td>Amory et al., 2002</td>
<td>3.54 (0.03 to ∞)</td>
</tr>
<tr>
<td>Amory et al., 2004</td>
<td>3.13 (0.03 to ∞)</td>
</tr>
<tr>
<td>Svartberg et al., 2004</td>
<td>0.30 (0.00 to 36.40)</td>
</tr>
<tr>
<td>Pooled OR (95% CI)</td>
<td>1.82 (0.78 to 4.23)</td>
</tr>
<tr>
<td>Fatal or Nonfatal MI OR=2.24</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 14 (testosterone), 7 (placebo)

Testosterone Therapy and Mortality in Older Males with High CVD Risk

Risk of Non-Fatal MI: Pre vs Post Testosterone Prescription

<table>
<thead>
<tr>
<th></th>
<th>All Ages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (N)</td>
<td>55,593</td>
</tr>
<tr>
<td>Pre-prescription</td>
<td></td>
</tr>
<tr>
<td>Cases</td>
<td>193</td>
</tr>
<tr>
<td>Rate per 1,000 PY (95% CI)</td>
<td>3.48 (3.02, 4.01)</td>
</tr>
<tr>
<td>Post-prescription</td>
<td></td>
</tr>
<tr>
<td>Cases</td>
<td>65</td>
</tr>
<tr>
<td>Rate per 1,000 PY (95% CI)</td>
<td>4.75 (3.72, 6.05)</td>
</tr>
<tr>
<td>Rate Ratio (post/pre) (95% CI)</td>
<td>1.36 (1.03, 1.81)</td>
</tr>
</tbody>
</table>

RR (95% CI): < 65 yrs 1.2 (0.8, 1.6)
≥ 65 yrs 2.2 (1.3, 3.7)

Vigen, JAMA, 2013

Finkle, PlosOne, 2014
No increase in MI with IM T treatment in Medicaid Database

Risk of Myocardial Infarction in Older Men Receiving Testosterone Therapy

Jacques Baillargeon, PhD, Randall J. Urban, MD, Yong-Fang Kuo, PhD, Kenneth J. Ottenbacher, PhD, OTR, Mukkala A. Raji, MD, Fei Du, MS, Yu-li Lin, MS, and James S. Goodwin, MD

Change in Non-Calcified Plaque over 12 m: T Trials

Synder, End Rev, 2018
Conclusions from T Trials

**ESSENTIAL POINTS**
- Testosterone treatment of 1 year for older men with low testosterone improved all aspects of sexual function
- Testosterone treatment of 1 year for older men with low testosterone improved walking distance by a small amount
- Testosterone treatment of 1 year for older men with low testosterone did not improve vitality but slightly improved mood and depressive symptoms
- Testosterone treatment of 1 year for older men with low testosterone improved hemoglobin and corrected mild to moderate anemia
- Testosterone treatment of 1 year for older men with low testosterone markedly increased the volumetric bone mineral density and estimated bone strength
- Testosterone treatment of 1 year for older men with low testosterone increased the coronary artery plaque volume
- Testosterone treatment of 1 year for older men with low testosterone was not associated with more cardiovascular or prostate adverse events however, the number of men and the duration of treatment were not sufficient to draw definitive conclusions about the risks of this treatment

Snyder, Endocrine Reviews, 2018

Case 1

- Prostate:
  - PSA 2.3
  - DRE normal
- ? CVD
  - CVD Risk Factors: HTN, +smoking, age, sex
  - TC 202, TG 176, HDL 66, LDL 101
Case 1

– Prostate:
  • PSA 2.3
  • DRE normal
– ? CVD
  • CVD Risk Factors: HTN, +smoking, age, sex
  • TC 202, TG 176, HDL 66, LDL 101
  • 10 year risk of MI/Stroke: 24%
  • On ASA, losartan

Case: Follow Up

• Hold on Testosterone Replacement
• Start atorvastatin 20 mg
• Consider switch off TDF and/or DRV/r
• Optimize Vitamin D and Calcium
• Smoking cessation
• Weight bearing exercise
• Repeat DXA in 1 year
Case 1: Take Home Points

- Presenting signs and symptoms of hypogonadism are non-specific
- Use quality free testosterone assays to make the diagnosis with a morning measurement
- Possible benefits needs to be weighed against possible risks
- Long-term safety unclear

Case 2

- 66 y/o AAF y/o with HIV presents for an initial visit for evaluation of diabetes:
  - Hemoglobin A1c 6.6%. Twin sister, brother, mother all have DM. BMI 23
  - Diagnosed with HIV in 2003, VL< 20 on TDF/FTC/ETV, CD4 cell count 374
  - Osteoporosis RF: + smoking, TAH age 21 with HRT until late 30s, h/o phenobarbital use for seizures, Mother with spine fractures. No falls, no personal h/o fracture
  - Drinks two cups of milk daily
  - Medical Problems: Bipolar, Asthma, Seizure d/o
To Screen or Not to Screen….

US National Osteoporosis Foundation (NOF) Guidelines for DXA Screening

• Those with a fragility fracture after age 50
• Women ≥ 65 yrs, Men ≥ 70 yrs
• Younger postmenopausal women and men 50-69 years with clinical risk factors for fracture
• Adults with a condition (e.g., rheumatoid arthritis) or taking a medication (e.g., glucocorticoids in a daily dose ≥ 5 mg prednisone or equivalent for ≥ three months) associated with low bone mass or bone loss
Case 2

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>-3.2</td>
<td>-1.2</td>
</tr>
<tr>
<td>Femoral Neck</td>
<td>-2.3</td>
<td>-1.0</td>
</tr>
<tr>
<td>Total Hip</td>
<td>-1.7</td>
<td>-0.7</td>
</tr>
</tbody>
</table>
Definitions

Operational 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

Case 2

• Recommended metformin
• Secondary work-up negative (nl TSH, 25D, FEPPhos, Ca++, nl PTH)
Case 2

What would you do to decrease her risk of fracture?

1. Switch off TDF and replace with TAF, abacavir or raltegravir and evaluate with DXA in 1 year
2. Start bisphosphonate therapy
3. Switch off TDF and start bisphosphonate therapy
4. Increase her vitamin D to 4000 IU daily.

How much would expect that a switch off of TDF will improve BMD?
Switch from TDF to ABC in Osteopenia/Osteoporosis
Changes in Spine and Hip BMD at Week 48

OsteoTDF Study

Two-centered, randomized pilot study in virologically suppressed subjects receiving TDF with osteopenia/osteoporosis. Twenty six subjects switched to ABC and 28 continued TDF.

In this small cohort, switching from TDF to ABC resulted in increases in hip and decreases in spine BMD at week 48.


Switch from TDF to RAL in Osteopenia/Osteoporosis
Changes in Spine and Hip BMD at Week 48

TROP Study (Switch): TDF to RAL

Open-label, non-randomized study comparing BMD changes at week 48 in patients with osteopenia/osteoporosis at baseline on TDF, switching to RAL with boosted PI (N=37).

In this small switch cohort, there are increases in spine and hip BMD at week 48.

Change in BMD and Bone Markers at Week 48 with Switch to RPV/DTG

### Adjusted Change From Baseline in Total Hip and Lumbar Spine BMD (g/cm²) at Week 48*

- **DTG + RPV, n=46**
- **CAR, n=35**

*Changes in total hip and lumbar spine BMD were consistent across subgroups (ie, age, sex, BMI, baseline third-agent class)*

**BSAP, bone-specific alkaline phosphatase; CTX, type 1 collagen cross-linked C-telopeptide; P1NP, procollagen type 1 N-propeptide.**

**BMD P values are from an ANCOVA model adjusted for baseline BMD, age at baseline, and baseline BMI.**

**Biomarker P values show comparisons between DTG + RPV and CAR at Week 48 for each marker, adjusted for baseline third-agent class, age, sex, BMI, smoking status, and baseline biomarker level. Statistical model uses log-transformed data.**

McComsey et al. IAS 2017; Paris, France. Poster TUPDE0205LB.
Pros

• Has osteoporosis of spine (higher relative risk of fracture)

Cons

• Relatively low absolute risk of fracture given age
• Switching may improve BMD
• Potential toxicities of BP
  – Gastrointestinal (oral)
  – Osteonecrosis of Jaw (rare)
  – Risk of oversuppression of bone turnover with long-term use → Atypical Femur fractures (rare)

Subclinical Vertebral Fracture in an Italian Cohort

2/3 of those with subclinical vertebral fractures did not have osteoporosis
Management:

- Plain films of thoracic and lumbar spine showed no occult fracture (50% of vertebral fractures are silent)
- Counseling re: exercise, smoking cessation, calcium (~1000-1200 mg/d) and vitamin D (~1000 IU/d) intake, fall risk reduction
- Switched to ABC/3TC/DTG and then to TAF/FTC + DTG

Case 2

Dual X-ray Absorptiometry: 15 months after TDF switch

<table>
<thead>
<tr>
<th></th>
<th>T-score</th>
<th>Z-score</th>
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</thead>
<tbody>
<tr>
<td>L1-L4</td>
<td>-3.2</td>
<td>-1.2</td>
</tr>
<tr>
<td>Femoral Neck</td>
<td>-2.1</td>
<td>-0.7</td>
</tr>
<tr>
<td>Total Hip</td>
<td>-1.5</td>
<td>-0.4</td>
</tr>
</tbody>
</table>

No Change  
↑ 6.6%  
↑ 3.7%

DM Update: Didn’t start metformin because of pill size. Saw Nutrition. A1c 5.9%
Treatment Options

- Bisphosphonates
  - Reduces vertebral & non-vertebral fractures by 25-50% in non-HIV
  - 6 RCT in HIV+ subjects in combination with calcium and vitamin D

<table>
<thead>
<tr>
<th>Author, year (N)</th>
<th>T-score</th>
<th>Medication (duration)</th>
<th>Spine</th>
<th>Hip</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guaraldi, 2004 (N=41)</td>
<td>&lt; -1.0</td>
<td>Alendronate 70 mg/wk (1 yr)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Mondy, 2005 (N=31)</td>
<td>&lt; -1.0</td>
<td>Alendronate 70 mg/wk (1 yr)</td>
<td>+5.2%</td>
<td>+1.3%*</td>
</tr>
<tr>
<td>McComsey, 2007 (N=82)</td>
<td>&lt; -1.5</td>
<td>Alendronate 70 mg/wk (1 yr)</td>
<td>+3.1%</td>
<td>+1.1%*</td>
</tr>
<tr>
<td>Rozenberg, 2012 (N=44)</td>
<td>&lt; -2.5</td>
<td>Alendronate 70 mg/wk (2 yrs)</td>
<td>+7.4%</td>
<td>+4.1%</td>
</tr>
<tr>
<td>Bolland, 2007 (N=43)</td>
<td>&lt; -0.5</td>
<td>Zoledronic acid 4 mg/year (2 yrs)</td>
<td>+8.9%</td>
<td>+2.6%*</td>
</tr>
<tr>
<td>Huang, 2009 (N=30)</td>
<td>&lt; -1.5</td>
<td>Zoledronic acid 5 mg/year (1 yr)</td>
<td>+3.7%</td>
<td>+0.7%*</td>
</tr>
</tbody>
</table>

* P < 0.05; † P < 0.001; NS = not significant


Considerations When Choosing Between Bisphosphonates

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

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Recommendations for Drug Holiday from Bisphosphonates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Category</td>
<td>Recommendation</td>
</tr>
<tr>
<td>High-risk: T-score still $\leq -2.5$ at the hip, previous fracture of the hip or spine or ongoing high-dose glucocorticoid therapy.</td>
<td>Drug holiday not justified.</td>
</tr>
</tbody>
</table>

Moderate risk: Hip bone mineral density value is now $>-2.5$ (T-score), and no prior hip or spine fracture. Consider drug holiday after 3-5 years of alendronate, risedronate, or zoledronic acid therapy. No information about ibandronate and drug holidays. Discontinue therapy.

Low-risk: Did not meet current treatment criteria at the time of treatment initiation. How long? How to monitor? What medications after the holiday?

McClung, Am J Medicine, 2013

Switch off TAF vs Bisphosphonate: ZEST Study

ZOL vs TDF switch for low BMD
Changes in BMD

- Lumbar spine
  - ZOL
  - TDF switch
  - Mean diff. 4.4\% (95\%CI 2.6-6.3); p=0.001

- Femoral neck
  - ZOL
  - TDF switch
  - Mean diff. 2.1\% (95\%CI 0.3-3.9); p=0.028

- Total hip
  - ZOL
  - TDF switch
  - Mean diff. 2.6\% (95\%CI 0.3-5.0); p=0.014

- 1 pt in ZOL group had unmeasurable hip BMD
- M12 data carried forward for 1 pt/group because of subsequent left hip replacements
- Baseline data carried forward to M12 for 1 patient in TDF switch group

Hoy, IAS, 2017
Case 2: Take-Home Points

- Screen with DXA all PM women and men >50 years. Prioritize those with additional RFs
- Switching off TDF improves T-score by about 0.2 SD.
- Switch alone vs switch + BPs depends on absolute fracture risk
- Consider lateral spine x-rays to further risk stratify
- Consider a drug holiday after >5 years of bisphosphonate use, especially if absolute risk is very high

Case 3

50 year old Caucasian male diagnosed with HIV in 1985, started antiretroviral therapy in 1995. Most recent CD4 cell count 236, viral load undetectable on TDF/FTC/LPV/r

Referred to Endocrine Clinic for fat accumulation in dorsocervical area
Case 3

• In the 3 years after initiation of highly active antiretroviral therapy (HAART), patient noticed thinning of his buttocks and legs

• In 3 months prior to presentation (~9 years after starting HAART), patient noticed the appearance of fat behind the neck and on the shoulders, facial fullness

• Also with some fatigue and weakness

“Is there anything else that is bothering you?”

Left hip pain for the past 2 weeks. No antecedent trauma
What test would you order?

1) MRI of the hip
2) Plain x-rays of the hip
3) Skeletal survey

Avascular Necrosis

- Incidence of symptomatic disease 100x higher in HIV-infected patients
- 4.4% of 339 asymptomatic patients at NIH
- Pathogenesis poorly understood
- Not associated with specific ARVs
- RFs: Steroid use, radiation, chemotherapy, sickle cell disease, trauma

Morse, CID, 2007
Femoral Neck Fracture

DXA Results

- Spine T-score: -2.6
- Right femoral neck T-score: -5.2
- Right total hip T-score: -4.2
Osteoporosis Risk Factors

– Steroid exposure
– ? Lactic acidosis/NRTI exposure
– Smoking
– Past heavy EtOH use

Secondary work-up:

- 25 OH Vit D 153 nmol/L
- PTH 15 ng/L
- Ca++ 2.5 mmol/L
- TSH 1.46 mU/L
- Testosterone 9.6 nmol/L
- Serum Phosphate 0.26 mmol/L

Fractional Excretion of Phosphate of 53%
1,25 dihydroxy Vitamin D 390 pmol/L (nl 15.6-161)
Management

• Tenofovir → Abacavir
• Phosphate 500 mg qid
• Calcium 1 gram tid

DXA Results: Follow Up

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<tr>
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<th>Baseline</th>
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<tbody>
<tr>
<td>Spine T-score</td>
<td>-2.6</td>
<td>-0.9</td>
</tr>
<tr>
<td>R femoral neck T-score</td>
<td>-5.2</td>
<td>-2.0</td>
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<tr>
<td>R total hip T-score</td>
<td>-4.2</td>
<td>-1.3</td>
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Change:
↑ 8.9%
↑ 5.5%
↑ 14.6%
Case 3: Take-Home Points

• All body fat changes in HIV-infected patients are not lipodystrophy
• Be aware of potential interactions between PIs (RTV) and all steroids given by all routes
• All low BMD is not osteoporosis
• Osteomalacia is an important cause of low BMD and should be investigated