Antiretroviral toxicities/complications of HIV infection

JOINT BASHH / BHIVA ONE DAY DIPLOMA IN HIV MEDICINE UPDATE

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13th Jan 2020
OSCEs

Dip HIV:

‘OSCE stations will test candidates on technical knowledge, clinical skills, clinical problem solving, clinical examination and management and counselling techniques’
General points on OSCEs

- Simulated patients/actors
- Common scenarios
  - Challenging clinic/ward round
- Reference guidelines if asked to
• Read the question-don’t lose focus
• Talk to the patient not the examiner
• Cover main points in history e.g. PMX/ risk
• Discuss options with the patient
• Give them opportunity to ask questions
• Formulate a clear plan at the end and check patient understands
Syllabus:

• Demonstrate competence at utilising routine laboratory tests to monitor the efficacy and safety of antiretroviral therapy;

• Explain the potential significant drug interactions between antiretroviral agents and drugs used for other indications

• Demonstrate knowledge of how different factors (e.g. significant co-morbidities like hepatitis or cardiovascular disease) may influence choice of antiretroviral therapies;

• **Recognise and manage toxicities associated with anti-HIV therapies, to include assessment and modification of risk factors for cardiovascular disease;**
Trends in new HIV diagnoses and in people receiving HIV-related care in the United Kingdom: data to the end of December 2018*
Overview

• Cardiovascular disease
• Renal
• Bone
• CNS
A growing number of people with HIV are reaching older age.
## POPPY Cohort

<table>
<thead>
<tr>
<th>PLWH &gt;50 years</th>
<th>PLWH &lt;50 years</th>
<th>HIV-ve &gt;50 years</th>
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<td>• N=1000</td>
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<td>• Aged ≥50 years</td>
<td>• Aged &lt;50 years</td>
<td>• Aged ≥50 years</td>
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<td>• White/black African ethnicity</td>
<td>• 150 aged 20-29, 30-39, 40-49 years</td>
<td>• Frequency matched on age, gender, ethnicity, sexual orientation and clinic</td>
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<tr>
<td>• Acquired HIV via sexual routes</td>
<td>• Frequency matched on gender, ethnicity, sexual orientation and clinic</td>
<td>• Frequency matched on age, gender, ethnicity, sexual orientation and geographical location (in/out London)</td>
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Non-AIDS medical events

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<th>PLWH&gt;50</th>
<th>PLWH&lt;50</th>
<th>HIV-ve &gt;50</th>
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<tbody>
<tr>
<td><strong>Cardiovascular events</strong></td>
<td>MI, angina, narrowed blood vessels, TIA, CABG. ( P=0.002 )</td>
<td>25% (76)</td>
<td>10% (14)</td>
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<tr>
<td><strong>Nervous system diseases</strong></td>
<td>Parkinson’s, vertigo, loss of consciousness, epilepsy, encephalitis. ( P=0.14 )</td>
<td>11% (35)</td>
<td>8% (11)</td>
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<tr>
<td><strong>Respiratory diseases</strong></td>
<td>Asthma, bronchitis, emphysema or COPD. ( P=0.004 )</td>
<td>42% (127)</td>
<td>26% (35)</td>
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Case 1

- 55 year old man CD4 350 Viral load < 50
- Stable on Kivexa/ Darunavir/Ritonavir
- Height 175 Weight 100kg (increased by 5 kg last 12 months)
- Fasting cholesterol 6.7, chol/HDL 3.5
- BP 145/90 (prev 130/80)
- Smokes 10/day
- HBA1c 35

- How do you manage this?
Case 1

- Do an annual cardiovascular risk assessment in all patients over 40

- Traditional risk factors

- HIV

- ART

- Abacavir
Case 1

BHIVA Monitoring guidelines (2016):

• We recommend that patients with established CVD and those at increased risk of CVD (10 year CVD risk >10%) are screened annually for hypertension, diabetes, dyslipidaemia and chronic kidney disease, and that BMI, smoking status and antiretroviral therapy are reviewed annually (GPP).

BHIVA ART guidelines 2015 (updated 2016)

• ‘one approach is to use the QRISK2 equation and apply a correction for HIV status of 1.6 (2D)’
Annual cardiovascular risk assessment

• Q RISK 2 = 11.8% x 1.6 = 18.88%
  – Referenced in BHIVA

• Q RISK 3 = 10.4% + SLE = 15.7%
  – More commonly used in practice
Prevention of Cardiovascular Disease (CVD)

Principles: The intensity of efforts to prevent CVD depends on the underlying risk of CVD, which can be estimated. The preventive efforts are diverse in nature and require involvement of a relevant specialist, in particular if the risk of CVD is high and always in persons with a history of CVD.

1. Assess CVD risk in next 10 years
   - Advise on diet and lifestyle in all persons
   - Consider ART modification if 10-year CVD risk ≥ 10%

2. Identify key modifiable risk factors
   - Smoking (see page 59)
   - Blood pressure
     - Drug treatment if: SBP ≥ 140 or DBP > 90 mmHg (especially if 10-year CVD risk ≥ 10%)
     - Target: SBP < 130 mmHg
       - Consider treating with acetylsalicylic acid 75-150 mg
     - Target: DBP < 80 mmHg

3. Coagulation
4. Glucose
   - Confirm DM and treat with diet and drugs
   - Target: HbA1c 6.5-7.0%

5. Lipids
   - Drug treatment if: established CVD or type 2 diabetes or 10-year CVD risk ≥ 10%
   - Target: LDL < 1.4 (55)
     - Treatment (see page 59)
   - Non-LDL < 2.2 (85)

6. Treatment (see page 80)
Cardiovascular disease prevention overview

NICE Pathways bring together everything NICE says on a topic in an interactive flowchart. NICE Pathways are interactive and designed to be used online.

They are updated regularly as new NICE guidance is published. To view the latest version of this NICE Pathway see:
Has to be taken in the context of multiple risk factors

- Age
- Male gender
- Family history of CHD
- Dyslipidemia (X 0.8 fold)
- Cigarette smoking (X 2.3 fold)
- Diabetes mellitus (X 2.3 fold)
- HIV (x 1.48)
- Hypertension (X 1.5 fold)

Non-modifiable

Modifiable

D:A:D Study: Smoking Cessation Reduces Risk of CVD in HIV-Infected Patients

- Cessation of tobacco smoking reduced risk of MI, coronary heart disease, and CVD in HIV-infected patients
  - No association of time since smoking cessation and mortality risk

*Adjusted for: age, cohort, calendar yr, antiretroviral treatment, family history of CVD, diabetes, time updated lipids and blood pressure assessments.
After adjustment* increased risk of myocardial infarction with use of abacavir and recent use of didanosine: D:A:D cohort 2009

Recent RR
yes/no
95% CI

Cumulative
RR per year
95% CI

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<th>Drug</th>
<th>#PYFU:</th>
<th>#MI:</th>
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<td>ddI</td>
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<td>ABC</td>
<td>53,300</td>
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<td>TDF</td>
<td>39,157</td>
<td>139</td>
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#PYFU = patients-years on study drug; #MI = number of myocardial infarctions.

*Adjusted for demographics, CV risk factors, and use of other antiretroviral drugs and further analyses included adjustment for latest measure of lipids, metabolic parameters, CD4, and HIV-RNA.

Recent use = current or within the last 6 months.

**Not shown (low number of patients currently on ddC).

ZDV = zidovudine; ddI = dideoxynosine; ddC = dideoxycytidine; d4T = stavudine; 3TC = lamivudine; TDF = tenofovir.

Lundgren JD, et al. 16th CROI. Montreal, Canada. 8–11 February 2009. Abstract LB44.
FDA meta-analysis of RCTs did not show an association between abacavir and MI

- 26 studies
- ABC: 24 MI events in 5,028 patients
- Non ABC: 22 MI events in 4,840 patients

Adapted from Ding X, et al. 18th CROI. Boston, MA. 27 February-2 March, 2011; Abstract 808.
D.A.D. Current Abacavir Use Associated With 98% Increase in Acute MI Risk

- Current ABC use remained associated with increased risk of acute MI
  - Similar RR in post-3/08 group vs pre-3/08 group, despite decrease in ABC use in pts with high CVD risk
  - Absolute risk in the post 2008 small: 6 cases/2000 PY vs 3 cases/2000 PY or absolute risk ↑ 0.15%
- Overall cohort: 941 MI events during 367,599 PYs
  - 0.47/100 PYs (95% CI: 0.42-0.52) with current ABC
  - 0.21 (95% CI: 0.19-0.22) with no current ABC

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<th>No Current ABC</th>
<th>Current ABC</th>
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<td>Events/PYs</td>
<td>600/295,642</td>
<td>341/71917</td>
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<td>Rate/100 PYs</td>
<td>0.20 (0.19-0.22)</td>
<td>0.47 (0.42-0.52)</td>
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<td>Adjusted Relative Rate of MI in Pts Currently Receiving ABC</td>
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<td>Overall</td>
<td>1.98 (1.72-2.29)</td>
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<td>Pre-3/08</td>
<td>1.97 (1.68-2.33)</td>
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<td>Post-3/08</td>
<td>1.97 (1.68-2.33)</td>
<td>1.97 (1.43-2.72)</td>
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Protease inhibitors and CVS risk

Incident rate ratio 1.59 (95% CI 1.33 to 1.91) for every 5 year use of DRV/rit

Lancet HIV 2018 5:e291-300
In individuals with a high CVD risk BHIVA

- We recommend use of alternatives to fosamprenavir/r and lopinavir/r
- We suggest that atazanavir/r is the preferred PI
- We suggest avoiding abacavir and maraviroc if an acceptable alternative is available.
- First-line ARV therapy with tenofovir-DF plus (emtricitabine or lamivudine) with dolutegravir or raltegravir or rilpivirine
# Antihypertensive Interactions

## Drug-drug Interactions between Antihypertensives and ARVs

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<th>ATVr</th>
<th>DRVc</th>
<th>DRVr</th>
<th>LPVr</th>
<th>DOR</th>
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</table>
### Statin interaction

![Lipid-Lowering Treatment Selector](https://www.hiv-druginteractions.org)

Charts revised December 2019. Full information available at [www.hiv-druginteractions.org](http://www.hiv-druginteractions.org)

<table>
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<tr>
<th>Statins</th>
<th>ATV/c</th>
<th>ATV/r</th>
<th>DRV/c</th>
<th>DRV/r</th>
<th>LPV/r</th>
<th>DOR</th>
<th>EFV</th>
<th>ETV</th>
<th>NVP</th>
<th>RPV</th>
<th>MVC</th>
<th>BIC/FTAF</th>
<th>DTG</th>
<th>EVG/c/FTAF</th>
<th>EVG/c/FTDF</th>
<th>RAL</th>
<th>ABC</th>
<th>FTC</th>
<th>F/TAF</th>
<th>TDF</th>
<th>ZDV</th>
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<tbody>
<tr>
<td>Aторвастатин</td>
<td>↑222%</td>
<td>↑190%</td>
<td>↑190%</td>
<td>↓2%</td>
<td>↓43%</td>
<td>↓37%</td>
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<td>Флуvasстатин</td>
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<td>1%</td>
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<tr>
<td>Питавастатин</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>26%</td>
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<tr>
<td>Прасвастатин</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>81%</td>
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<tr>
<td>Росувастатин</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>242%</td>
<td></td>
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<tr>
<td>Симвастатин</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>68%</td>
<td></td>
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</tbody>
</table>

| Fibrates              |       |       |       |       |       |     |     |     |     |     |     |          |     |           |            |     |     |     |       |      |     |
| Бэзафibrate           |       |       |       |       |       |     |     |     |     |     |     |          |     |           |            |     |     |     |       |      |     |
| Клофibrate            |       |       |       |       |       |     |     |     |     |     |     |          |     |           |            |     |     |     |       |      |     |
| Фенфibrate            |       |       |       |       |       |     |     |     |     |     |     |          |     |           |            |     |     |     |       |      |     |
| Гемфибrozил           |       |       |       |       |       |     |     |     |     |     |     |          |     |           |            |     |     |     |       |      |     |

| Other                  |       |       |       |       |       |     |     |     |     |     |     |          |     |           |            |     |     |     |       |      |     |
| Еволовумаб            |       |       |       |       |       |     |     |     |     |     |     |          |     |           |            |     |     |     |       |      |     |
| Эзетимиб              | ↑     | ↑     | ↑     | ↓     |       |     |     |     |     |     |     |          |     |           |            |     |     |     |       |      |     |
Case 1

- 55 year old man CD4 350 Viral load < 50
- Stable on Kivexa/ Darunavir/Ritonavir
  - Switch off Abacavir and PI
- Height 175 Weight 100kg (increased by 5 kg last 12 months)
  - Lose weight
- Fasting cholesterol 6.7, chol/HDL 3.5
  - Lipid management
- BP 145/90 (prev 130/80)
  - Monitoring +/- management
- Smokes 10/day
  - Stop smoking
- HBA1c 35

- How do you manage this?
Case 1 – what do you need to know?

- BHIVA ART guidelines
- Role of traditional risk factors
- Increased risk of CVD with HIV
- Lipid profile for ARVs
- Evidence from cohort studies
  - DAD data: PI/r versus NNRTI
  - DAD data: abacavir
- Drug–drug interactions for statins and anti-hypertensives
Case 2

- 50 year old woman
- VL < 50 CD4 445
- On Truvada/ Atazanavir
- Creat 110
- eGFR 65
  - Declined in renal function > 5ml/ yr
- UPCR 45
• Traditional risk factors
  – BP/ DM/ Hep
• HIV and kidney disease
• Renal monitoring
• Renal effects of ART
• Prescribing in renal failure
Prevalence of chronic kidney disease increases with age: non-HIV populations


GFR (ml/min/1.73 m²):  
- 45–59
- 30–44
- < 30

GFR = glomerular filtration rate.
Over an ~3-year period, 3.3% of patients on HIV therapy progressed to chronic kidney disease: EuroSIDA

- N = 6,843 (consecutive weights and creatinine recorded)
- Median follow-up 3.7 years (IQR 2.8–5.7)
- 225 (3.3%) progressed to CKD*
- Incidence 1.05 per 100 patient-year follow-up

* CKD defined as confirmed (persisting for 3 months) decrease to eGFR ≤ 60 ml/min/1.73 m² if eGFR at baseline > 60 ml/min/1.73 m², or confirmed 25% decrease in eGFR if baseline eGFR ≤ 60 ml/min per 1.73 m².

Early stages of chronic kidney disease are clinically silent.
HIV patients with mildly reduced eGFR* (60-89 ml/min/1.73^2) are at risk of progression to stage 4/5 chronic kidney disease: UK CHIC cohort

> Adjusted HR$ for progression to stage 4/5 CKD

<table>
<thead>
<tr>
<th>eGFR ml/min/1.73 m^2</th>
<th>Increased stage 4/5 CKD risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 90</td>
<td>1</td>
</tr>
<tr>
<td>60-89</td>
<td>3.6‡</td>
</tr>
<tr>
<td>59-30</td>
<td>95.2†</td>
</tr>
</tbody>
</table>

*eGFR 60–89 ml/min/1.73 m^2, eGFR calculated using the Chronic Kidney Disease Epidemiology Collaboration Formula (CKD-EPI); † p < 0.001; ‡ p = 0.002; § sub-distribution hazard ratio. Adjusted for age, ethnicity, risk group, AIDS, years since cohort entry, CD4 count, HIV RNA level, cART use, HBsAg, and hepatitis C virus status.*

## EuroSIDA: risk for incidence of chronic kidney disease

<table>
<thead>
<tr>
<th>Drug</th>
<th>IRR</th>
<th>95% C.I.</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atazanavir</td>
<td>1.21</td>
<td>1.09–1.34</td>
<td>0.0003</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>1.16</td>
<td>1.06–1.25</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Indinavir</td>
<td>1.12</td>
<td>1.06–1.18</td>
<td>&lt;0.0001</td>
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<tr>
<td>Lopinavir/r</td>
<td>1.08</td>
<td>1.01–1.16</td>
<td>0.03</td>
</tr>
<tr>
<td>Abacavir</td>
<td>1.04</td>
<td>0.98–1.09</td>
<td>0.16</td>
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</table>

Concomitant use of atazanavir and tenofovir resulted in a 41% increased incidence of CKD per year of additional exposure [IRR 1.41, 95% CI 1.24–1.61, p < 0.0001]

- CKD defined as confirmed (persisting for 3 months) decrease to eGFR ≤ 60 ml/min/1.73 m² if eGFR at baseline > 60 ml/min/1.73 m² or confirmed 25% decrease in eGFR if baseline eGFR ≤ 60 ml/min per 1.73 m².
- IRR = incidence rate ratio
- eGFR = estimated glomerular filtration rate.
- * Adjustment for traditional factors associated with CKD and other confounding variables

Tenofovir renal toxicity

- Affects proximal renal tubule
- Produces Fanconi like syndrome
- Proteinuria
- Renal impairment
- Phosphaturia/low phosphate
- Accumulation of metabolite in mitochondria
• Prodrug pharmacology
  Tenofovir Disoproxil Fumarate and Tenofovir Alafenamide

TAF results in >90% lower TFV plasma levels compared to TDF

OAT, organic anion transporter; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TFV, tenofovir.

Proteinuria

Screening and investigation for proteinuria

Urinary dipstick for protein

+ve

-ve

Routine clinical follow up

Always consider:
- Metabolic syndrome
- Hypertension
- Diabetes
- HIV AN
- Drug effects

uPCR <30 (nil else)

Annual renal screen

Renal work-up

? Renal referral

? Biopsy

uPCR >30
Or Haematuria
Or Ultrasound abnormal
Or eGFR <60 ml/min

Adapted from EACS Guidelines 2011. Available at:
http://www.europeanaidclinicalsociety.org/guidelines/ (accessed May 2011)
UPCR and ACR

• The Albumin-Creatinine Ratio, ACR for microalbuminuria
  – Diabetic nephropathy, Hypertension, Glomerulonephritis, HIVAN

• Total Protein-Creatinine ratio, TPCR (mg/mmol) indicates both glomerular and tubular protein leakage.

• High TPCR + normal ACR = tubular damage which can be a feature of drug induced e.g Tenofovir
Switching off Tenofovir

Clinical Commissioning Policy: Tenofovir Alafenamide for treatment of HIV 1 in adults and adolescents

Tenofovir disoproxil contra-indications
- CKD 1-3 as per NHSE policy update
- FRAX- ‘High risk of major fracture’ or D vexa T score <-2.5

Reference: NHS England: 16043/P
Switch study TDF to TAF
GS-US-292-0109

Each difference between treatment arms was statistically significant (p < 0.001).

Mills A, IAS 2015, Vancouver
## Atazanavir and renal stones

<table>
<thead>
<tr>
<th></th>
<th>ATZ</th>
<th>EFV/ DRV/r/ LPV/r</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients with RS</td>
<td>24 (2%)</td>
<td>24 (0.4%,0.6%,0.6%)</td>
<td></td>
</tr>
<tr>
<td>Prevalence RS: per 1000 patients (95% CI)</td>
<td>20 (13-30)</td>
<td>5.4 (3.2-7.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Event rate / 1000 pt yr of ARV exposure n (95% CI)</td>
<td>7.3 (4.7-10.8)</td>
<td>1.9 (1.2-2.8) 1.5, 4.5, 1.9</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Other causes of raised creatinine

• Creatine gym supplements
• **Dolutegravir and cobicistat** are known to decrease tubular section of creatinine without affecting glomerular filtration.
• Happens at initiation/ 2-3 weeks then stabilises
Renal adjustment of lamivudine

<table>
<thead>
<tr>
<th>Creatinine clearance (ml/min)</th>
<th>First dose</th>
<th>Maintenance</th>
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</thead>
<tbody>
<tr>
<td>≥50</td>
<td>300 mg</td>
<td>300 mg OD or 150mg BD</td>
</tr>
<tr>
<td>30-50</td>
<td>150 mg</td>
<td>150 mg OD</td>
</tr>
<tr>
<td>15 – 30</td>
<td>150 mg</td>
<td>100 mg OD</td>
</tr>
<tr>
<td>5 - 15</td>
<td>150 mg</td>
<td>50 mg OD</td>
</tr>
<tr>
<td>&lt;5</td>
<td>150 mg</td>
<td>25-50 mg OD</td>
</tr>
</tbody>
</table>
Case 2

- 50 year old woman from south Africa
- VL < 50 CD4 445
- On Truvada/ Atazanavir
  - Change treatment poss TAF/ Abac and switch off Atazanavir
- Creat 110
- eGFR 65
  - Declined in renal function > 5ml/ yr
- UPCR 45
  - Check ACR
  - Renal screen –autoimmune/ BP+/- USS
Case 2 – what do you need to know?

- Traditional risk factors for CKD
- Characteristics and pathogenesis of tenofovir associated renal toxicity: - proximal renal tubule dysfunction
- Screening tests for TDF toxicity and PRT dysfunction
- Indications for TAF
- Renal toxicity of atazanavir: interstitial nephritis, renal stones
- Assessment of proteinuria: glomerular v tubular
- Renal toxicity of atazanavir: interstitial nephritis, renal stones
- Other causes of raised creatinine
- Prescribing in renal failure
- Indications for TAF
- HIV associated renal disease HIVAN/ HIVICK
Case 3

- 55 year old post menopausal woman
- Stable on Truvada/ Raltegravir
- VL < 50 CD4 380
- ED : Fall and # wrist
- Normal calcium/ ALP/Phosphate
BHIVA Monitoring guidelines:

- FRAX score is calculated, and a history of falls elicited, in all patients >50 years
- < 10% fracture risk reassure and repeat in 3 years
- 10-20% provide lifestyle advice and optimise risk factors including vitamin D deficiency;
- >20%: optimise risk factors, review ART (TDF) and lifestyle factors, and refer for osteoporosis treatment.
BMD decreases with age

Relative influence on peak bone mass (men):
40–83% genetic
27–60% environmental

0.5–1% reduction in bone vol/year

Risk factors for osteoporosis

Traditional
- Female sex
- Older age
- Oestrogen deficiency
- White race
- Low weight
- Family history of osteoporosis
- Smoking
- History of fractures

HIV
- HIV
- ARV therapy
- Corticosteroids
- Decreased physical activity
- Malnutrition
- History of severe wasting
- Decreased muscle mass
- Decreased fat mass
- Fat deposition in marrow
- Liver disease
- Hypogonadism
- Amenorrhea or premature menopause
SUN Study
Prevalence of Osteopenia/Osteoporosis in HIV+ Patients

- Prospective study of 525 HIV+ patients with baseline DEXA bone densitometry compared with matched pairs from NHANES
  - Longitudinal follow-up ongoing
- ↑ in reduced bone density at the femoral neck in HIV+ vs controls
  - Osteopenia: 51.7% vs 29.1%
  - Osteoporosis: 9.8% vs 1.0%

![Comparison of Femoral Neck T-Scores Among SUN Study Participants and Matched Controls](chart.png)

### Multivariate Analysis: Factors Related to Osteoporosis

<table>
<thead>
<tr>
<th>Factor</th>
<th>OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &lt;22.5 kg/m²</td>
<td>3.01 (2.24-5.69)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Age &gt; 45 years</td>
<td>2.35 (1.33-4.15)</td>
<td>.003</td>
</tr>
<tr>
<td>BL CD4+ &lt;300</td>
<td>2.10 (1.16-3.78)</td>
<td>.013</td>
</tr>
<tr>
<td>HIV &gt; 97.7 mos</td>
<td>1.56 (1.09-3.55)</td>
<td>.023</td>
</tr>
</tbody>
</table>
BMD in patients initiating ART

- Significant greater bone loss with TDF/FTC vs. ABC/3TC (ACTG 5202)
Switching off Tenofovir

Clinical Commissioning Policy: Tenofovir Alafenamide for treatment of HIV 1 in adults and adolescents

Reference: NHS England: 16043/P

Tenofovir disoproxil contra-indications
- CKD 1-3 as per NHSE policy update
- FRAX- ‘High risk of major fracture’ or Dexa T score <-2.5
TAF - Changes in Spine and Hip BMD Through Week 48
Studies 104 and 111: Week 48 Combined Analysis

<table>
<thead>
<tr>
<th>Week 0</th>
<th>Week 24</th>
<th>Week 48</th>
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<tbody>
<tr>
<td>Hip</td>
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<tr>
<td>E/C/F/TAF, n</td>
<td>836</td>
<td>789</td>
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<td>E/C/F/TDF, n</td>
<td>848</td>
<td>815</td>
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<table>
<thead>
<tr>
<th>Spine</th>
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<td>E/C/F/TAF, n</td>
<td>845</td>
<td>797</td>
</tr>
<tr>
<td>E/C/F/TDF, n</td>
<td>850</td>
<td>816</td>
</tr>
</tbody>
</table>

Mean (SD) % Change from Baseline

Week 0: 0
Week 24: -0.66
Week 48: -2.95

Week 0: 0
Week 24: -2.86
Week 48: -1.30

p < 0.001

Sax P. CROI 2015, Seattle
Case 3

• 55 year old post menopausal woman
  – ? Other signs of menopause ? HRT
• Stable on Truvada/ Raltegravir
  – Change off Tenofovir
• VL < 50 CD4 380
• ED :Fall and # wrist
• Normal calcium/ ALP/Phosphate
Management of osteoporosis: general measures

• Adequate nutrition with maintenance of normal body weight
• Adequate calcium intake (around 1g/day), dietary or as supplement
• Vitamin D repletion if required (up to 2,000 IU/day)
• Stop smoking and avoid alcohol abuse
• Encourage physical activity
• Avoid falls
Case 3 – what do you need to know?

- Traditional risk factors for osteoporosis
- Assessment of fragility fracture risk: FRAX score
- Increased risk of osteopaenia/osteoposis in HIV.
- Association with reduction of some ARVs with reduced BMD
- Management of osteoporosis
  - NICE guidelines
Case 4

- 35 year old man CD4 625 Viral load <20
- On Atripla 2yrs

Feeling depressed
Not sleeping well
Asks if it could be the drugs?
Case 4

BHIVA ART guidelines 2015 (updated 2016)

• **What to start:** we recommend that efavirenz-containing regimens be avoided in individuals with a current or past history of depression, psychosis, suicidal ideation or attempted suicide, or at risk of self-harm (1C).

• **Switching therapy:** we recommend that efavirenz-containing regimens should be switched promptly to a viable alternative when PLWH present with depression, psychosis, suicidal ideation or attempted suicide, or self-harm (1C).
BHIVA

- screening for the presence of symptoms of depression, anxiety, drug and alcohol misuse, acute stress disorder and risk of self-harm 3 months of receiving an HIV diagnosis.
- repeated screening following events that are known to trigger or exacerbate psychological distress or cognitive difficulties, and otherwise on an annual basis
- should be offered referral to a suitably competent practitioner for further assessment
SENSE: Neuropsychiatric AE prevalence (ITT) grade 1-4, at least possibly related to study drug.
Efavirenz and CNS toxicity

472 patients started on Atripla
About 1/5th patients discontinued in 12 months
CNS toxicity was most common reason (63 patients, 71%)

Scourfield A et al. AIDS. 2012 Mar 23. [Epub ahead of print]
Mental health problems in HIV

• CHARTER study:
  – 1,555 individuals
  – Over 50% patients had mental health problems

• In the UK over 20% have mild to moderate neurocognitive impairment

• Asymptomatic neurocognitive impairment can be important clinically

• Patients on HAART with undetectable viral load may have cognitive involvement
Retrospective analysis of cohort of ~3,000 HIV-positive individuals in The Netherlands in 2004 calculated the percentage of individuals who had discontinued DTG.

- Treatment discontinuation due to AEs with DTG

Subjects with AEs (%)

- Sleeping disturbance: 19/387
- Gastrointestinal issues: 18/387
- Neuro-psychological issues: 12/387
- Fatigue: 9/387
- Headache: 8/387
- Paresthesia: 6/387
- Allergy: 1/387
- Others: 5/387

Adapted from: Brinkman K et al. CROI 2016. Boston, MA. #948
# Antidepressant Treatment Selector

Charts revised November 2017. Full information available at [www.hiv-druginteractions.org](http://www.hiv-druginteractions.org)

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Case 4

- 35-year-old man CD4 625 Viral load <20
- On Atripla 2yrs
- Switch to an alternative
- Full mental health history including chems
- Talking therapies – clinic/ GP/ 3rd sector
- Consider drug-drug interactions including OTC if needs antidepressants

Feeling depressed
Not sleeping well

Asks if it could be the drugs?
Case 4 – what do you need to know?

- Assessment of depression
- Management and treatment options for depression
- Mental health problems and adherence
- Neuropsychiatric symptoms associated with ARVs
- Evidence from switch data for managing efavirenz neuropsychiatric symptoms
- Tolerability of other 3rd agents
- Drug-drug interactions: ARVs and anti-depressants
Summary

- HIV patients are living longer and are at greater risk of non-HIV co-morbidities
- Long-term toxicities of ART may have an impact on those co-morbidities
- Treatment choice should tailored to the patient and dynamic to their needs
- Remember basic assessment and management of common risk factors first and then move onto ART changes