Cardiovascular disease in HIV

Loice Achieng,
University of Nairobi, Kenya
Conflict of interest

• None that is relevant to this presentation
This presentation will revolve around a case
Case presentation

- 53 year old Kenyan male
- Has been in care for HIV since 2005 though I first saw him about 2 weeks ago
- Current ART regimen of AZT/3TC/LPVr
- Known to have hypertension and is on treatment
- Smoker for several years but has recently reduced to 2-3 cigarettes/day
- Creatinine clearance of 65ml/min
- Dyslipidaemia
- HbA1C 7%
Discussion points

1. Is this patient unique?

2. What is his cardiovascular disease risk stratification?

3. What is the appropriate ART for him?

4. Does he require a statin?

5. How else can his CVD risk be reduced?
HIV Patients are Aging

- Projected age distribution of HIV patients on ART 2010-2030
- National Dutch ATHENA cohort with data between 1996 and 2010
- Median age will increase from 43.9 years in 2010 to 56.6 in 2030
- Proportion of HIV patients over 50 will increase from 28% in 2010 to 73% in 2030

HIV Patients will Face Increased Rates of NCDs as they Age

- Predicted burden of non-communicable diseases (NCDs) in HIV patients modeled for 2010-2030
- NCDs include
  - Cardiovascular disease (hypertension, hypercholesterolemia, myocardial infarction, stroke)
  - Diabetes
  - Chronic kidney disease
  - Osteoporosis
  - Non-AIDS malignancies

HIV Patients will Face Increased Rates of NCDs compared with HIV-negative

- Projected distribution of NCDs by age group in HIV versus non-HIV in 2030

Kenya

- Mean age of populations in our clinic is 44-45 years, up from a mean of 37 years in 2006.
Increasing prevalence of traditional CVD risk factors

- Kenya - Dyslipidemia in unto 65% of patients on ART, hypertension in 35% of the HIV population compared to 23% in a non HIV population of comparable age, low smoking rates, >50% overweight

- Johannesburg - Dyslipidaemia rates of unto 45%, hypertension in 19.1%

Julius H, Basu D et al. The burden of metabolic diseases amongst HIV positive patients on HAART attending the Johannesburg Hospital. Curr HIV Res 2011 June; 9(4)

Harunany, Achieng et al 2017 - unpublished data
In largely female populations

- Gender has not been shown to be a specific risk factor for CVD in HIV infected populations

- HIV infected women have been shown to have increased rates of AMI and ischemic stroke rates compared to HIV-uninfected women and men

- Persisting inflammation may explain the observed increase

Cardiovascular complications of HIV ART and myocardial infarction

MI incidence according to duration of ART exposure

Age/race-ethnicity adjusted rates of acute myocardial infarction (AMI) by cardiovascular disease risk factor profile (CVDRF) stratified by HIV status

HR= Hazard Ratio**p-value for this hazard ratio was 0.044

Discussion points

1. Is this patient unique?

2. What is his cardiovascular disease risk stratification?

3. What is the appropriate ART for him?

4. Does he require a statin?

5. How else can his CVD risk be reduced?
Risk stratification

- Multiple risk stratification calculations including Framingham Risk Score, D:A:D score, ASCVD and others

- Most thought to underestimate CVD risk since they do not incorporate factors unique to HIV such as effects of ART, immune activation etc

- ASCVD may accurately correlate with observed artherosclerotic disease

CVD Outcomes Underestimated in HIV-Positive Pts by Risk Calculators

- CVD risk scores calculated with data from 2006-2009 for pts in Partners HealthCare System Cohort\(^1\)

- Analysis of HOPS cohort (n = 2283) found FRS accurately estimated CVD risk but AHA/ACC and D:A:D underestimated risk\(^2\)

Performance of risk calculators in African settings

- ASCVD accurately identified high risk patients compared to cIMT
- ASCVD identified more patients as having a higher risk score than FRS
ACC/AHA 2013 Cardiovascular Risk Assessment

Input:
- Race: African American
- Sex: Male
- Age: 53 yr
- Total Cholesterol: 6.3 mmol/L
- HDL Cholesterol: 0.9 mmol/L
- Systolic Blood Pressure: 138 mmHg
- On Hypertension Med: No
- Diabetes: Yes
- Smoker: Yes

Results:
- Ten Year Risk: 38.07 %
- Decimal Precision: 2
Discussion points

1. Is this patient unique?

2. What is his cardiovascular disease risk stratification?

3. What is the appropriate ART for him?

4. Does he require a statin?

5. How else can his CVD risk be reduced?
Effects on Lipids of various ART

- TDF
- RAL
- DTG
- RPV
- ETV
- ABC
- EFV
- ATV/RTV or ATV/COBI
- DRV/RTV or DRV/COBI
- EVG/COBI
- LPVr
- AZT

Adapted from CCO
Switch to safer drug?

• The goal of switching would be to transition to a safe regimen without loss of viral suppression or introduction of new ADR
ATAZIP Study: Switch LPV/r to ATV/r

Time to treatment failure and time to virological failure did not differ between groups

The median changes in CD4 count at 48 weeks were +27 cells/mm$^3$ (IQR: -42 to 119) with ATV/r and +48 cells/mm$^3$ (IQR: -5 to 112) with LPV/r (p = 0.315)

Mallolas J, JAIDS 2009;51:29-36
ATAZIP Study: Switch LPV/r to ATV/r

Fasting plasma lipids changes from baseline to week 48

- Triglycerides: p < 0.001
- Total cholesterol: p < 0.001
- LDL cholesterol: p = 0.149
- HDL cholesterol: p = 0.185

Mallolas J, JAIDS 2009;51:29-36

Switch to ATV/r 300/100 qd (N = 121)
Continue on LPV/r 400/100 bid (N = 127)
NRTI sparing?

- Abacavir - some studies showing increased association with AMI, recommendations to avoid in high risk for CVD

- TDF - Renal insufficiency

- AZT - Increase lipodystrophy and lipid abnormalities
Switch to INSTI?

- INSTIs - Lipid neutral
- Most studies look at switch from a first line regimen
- DAWNING STUDY
- Switch to INSTI in virologically suppressed treatment experienced patients with possible archived mutations

Does the patient need a statin?


Effects of Statin Therapy on Coronary Artery Plaque Volume and High Risk Plaque Morphology in HIV-Infected Patients with Subclinical Atherosclerosis: a Randomized Double-Blind Placebo-Controlled Trial

Lo J et al
Atorvastatin on coronary plaque volume

Figure 2. Comparison of the 1-Year Change in Noncalcified Plaque Volume in HIV Patients Randomized to Atorvastatin vs. Placebo

Horizontal line in center of box denotes median and top of box denotes 75th centile and lower end of box denotes 25th centile.
Atorvastatin on LDL

Figure 4. Comparison of the 1-Year Change in Direct LDL in HIV Patients Randomized to Atorvastatin vs. Placebo
Bars represent means and error bars represent standard deviations.
What statin to use - INTREPID TRIAL

- Pitavastatin VS Pravastatin associated with lower fasting LDL cholesterol

- Pitavastatin vs Pravastatin associated with greater reduction in selected markers of immune activation and arterial inflammation (sCD14, oxLDL, IpPLA2)

Aberg J. Lancet HIV 2017 July: 4(7)e284

Torbio M et al. AIDS 2017 March 27; 31(6):717-806
Can statins prevent CVD events

- On-going REPRIEVE trial

- Patients on ART for at least 6 months, randomised to either pitavastatin or placebo and follow-up for 3.5-6 years depending on when they enrol

- Outcome - Time to the first event of a composite of major cardiovascular events

- Results expected in 2020
How else can we reduce his CVD risk

CVD hazard in D:A:D*
Reduce sysBP 10 mmHg
Reduce TC 1 mmol/L
Stop smoking

*relative to 40 y.o. HIV+ male

Petoumenos K for D:A:D . 20^{th} CROI 2013.
Interventions to reduce fat and inflammation

- Blocking microbial translocation (Rifaximin) – no reduction in LPS
- Anti-inflammatory agents – statins
- Chloroquine – modest reduction in CD8 T-cell activation
- Aspirin – Aspirin fails to impact immune activation or endothelial function in treated HIV
  - In a trial looking at different doses of ASA vs placebo, ASA had no effect on sCD14, FMD, sCD163, D-dimer
For HIV programs
What is our measure of success in HIV treatment?

- 90-90-90 the new goal
- Number tested
- Number initiated on ART
- Number with virologic suppression
- Number retained
- Number started on IPT
- Septrin use
- Perinatal transmission
Time for a new metric

• NCD just as important as the HIV
Ageing with HIV: Clinical consequences

Causes of death in a successfully ART-treated population:

- CVD: 31%
- Cancer*: 19%
- Unnatural**: 18%
- Infection: 10%
- Liver disease: 8%
- AIDS: 3%
- Unknown: 2%

* = non-AIDS malignancy
** = accident, suicide or violent death

Where resources are scarce, what should be the priority

• Model from the Athena cohort predicts that annual CVD incidence and costs will increase by 55% and 36% between 2015-2030.

• Smoking cessation and intensified monitoring and treatment of hypertension and dyslipidaemia, will avert the largest number of annual CVD cases (13.1% and 20.0%)

What is feasible

- SEARCH HIV test and treat study - in 10 rural communities in Uganda
- 193 HIV infected adults with NCD, mostly hypertension, referred for care
- Composite end point of both HIV and Hypertension control after 2 years achieved in 67% of the patients
- This is the context of intentional screening
HIV Provider-Patient Communication Regarding Cardiovascular Risk:

- Results from the 2010 AIDS Treatment for Life International Survey.
- Only 19% of patients had ever discussed heart disease with their HIV clinician.
- <30% ever discussed hypertension, cholesterol, family history or smoking with clinician.
- 44% of patients who smoked reported never having discussed this with a clinician.
- <30% ever discussed CVD risks of ART with clinician.

What happened to our patient?
Unconfirmed Diagnosis

>>> Acute MI <<<

Fac: Accident & Emer>
Summary

- Our patients get CVD
- Appropriate screening and management will avert many CVD events
- Traditional risk factors still the most common and preventable cause
- We should change our metric for measuring control of HIV disease
Thank you