Evolution of Cardiovascular Disease in the HIV patient

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47 y Latino Referred for Evaluation of Chest Tightness and Exercise Intolerance

- Several months of chest tightness, palpitations and fatigue with moderately-intense activity
- HIV infection 1998; Treatment delayed 1999
- Chronic infections with genital herpex simplex and hepatitis B
- AV nodal reentry tachycardia – S/P ablation
- Treatment with dolutegravir, abacavir/lamivudine/tenofovir
Diagnostic Studies

- Echocardiogram – mild to moderate hypocontractility of apex/apical septum; LVEF = 48%; reduced LV compliance
- Stress echocardiogram – no inducible ischemia
- Holter – isolated APBs
- FBG 102 mg/dL, Cr 1.61 mg/dL (eGFR 55.8 mL/min/1.73 m², ALT 27 U/L, TSH 1.54 μIU/mL
- NMR LipoProfile
  TC 171 mg/dL, HDL-C 27 mg/dL, TG 409 mg/dL
  Non-HDL-C
  LDL-P 1579 nmol/L, HDL-P 22 μmol/L
- Lp(a) 175 mg/dL
Objectives

• Discuss the evolution in cardiovascular disease in HIV patients

• Review lipoprotein abnormalities associated with HIV infection and HAART therapy and their importance in cardiovascular risk assessment.

• Discuss the limitations of current lipid modifying therapy in HIV patients
Cardiovascular Complications in HIV Pre-ART Era

Dilated Cardiomyopathy

• Prevalence 10-30% based on echocardiographic, observational and autopsy studies\(^1\)
• Associated with significantly reduced CD4 T-cell count\(^1\)
• Poor prognosis than those without DCM (101 days (95% CI: 42-146) vs. 472 days (95% CI: 383-560)\(^2\)
• Pathogenesis:
  – Direct infection by HIV
  – Opportunistic infections (toxoplasmosis)
  – Mitochondrial dysfunction by non-nucleoside reverse transcriptase inhibitors (NNRTI)
  – Circulating toxins
  – Toxicity of alcohol, illicit or self-prescribed substances
  – Nutritional disorders

Cardiovascular Complications in HIV Pre-ART Era

Pericardial Disease

- Frequency between 5% and 46% with incidence of 11-17% per year\(^1,2\)
- Associated with significantly reduced CD4 T-cell count\(^1\)
- Pathogenesis:
  - Opportunistic infections
  - Malignancy

Post-ART Era:

- Control of herpes virus 8 and Epstein-Barr virus infection, which are both associated with HIV-related tumors, have contributed to the reduced incidence of pericardial effusion in HIV-infected patients in recent years

Cardiovascular Complications in HIV Pre-ART Era

Pulmonary Arterial Hypertension (PAH)

- Prevalence 1/200 HIV-infected patients vs 1/200,000 in general population
  
  - Devastating, progressive disease associated with severe cardiac impairment, poor quality of life, right ventricular failure and death
  
  - Occurs in HIV-infected patients without predisposing risk factors such as intravenous drug use, thromboembolic disease or pulmonary infection
  
  - More common in young men (mean age 32 y)

- Pathology of HIV-associated PAH shares similarities with PAH of different etiologies

- Prevalence has not changed in ART era. Risk associated with drug use, homosexuality and hemophilia

MI Rates in HIV- and Non-HIV-Infected Patients

Anti-Retroviral Therapies

- Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
- Non-nucleoside reverse transcriptase inhibitors (NNRTI)
- Protease inhibitors (PI)
- Fusion Inhibitor
- Integrase Inhibitors
- CCR5 Anatagonist
Changes in Antiretroviral Drug Use and Vascular Events

Use of Antiretroviral Drugs

Vascular Events and Death

## Risk of Events Related to Exposure to Antiretroviral Drugs

<table>
<thead>
<tr>
<th>Antiretroviral Drug or Combination</th>
<th>All Cause Death</th>
<th>Admission for CVD or CVAD or All Cause Death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)*</td>
<td>P-Value*</td>
</tr>
<tr>
<td>NRTI</td>
<td>0.67 (0.62 – 0.72)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PI</td>
<td>0.54 (0.47 – 0.61)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NNRTI</td>
<td>0.62 (0.50 – 0.77)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NA + PI</td>
<td>0.36 (0.32 – 0.41)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NA + NNRTI</td>
<td>0.41 (0.33 – 0.52)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Comparing events related to exposure for 24 months vs 0 months

NRTI = nucleoside reverse-transcriptase inhibitor; PI = protease inhibitor; NA = nucleoside analogue
NNRTIs = nonnucleoside reverse-transcriptase inhibitor
CVD = cardiovascular disease; CVAD = cerebrovascular disease

Factors That Potentially Influence Cardiovascular Risk in HIV Patients

<table>
<thead>
<tr>
<th>Increase Cardiovascular Risk</th>
<th>Decrease Cardiovascular Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyslipidemia, insulin resistance, body habitus changes associated with HIV itself and certain components of ART</td>
<td>Control of viral replication with ART improves endothelial function</td>
</tr>
<tr>
<td>High rates of other cardiovascular risk factors, in particular smoking</td>
<td>Current antiretroviral regimens have more favorable effects on metabolic parameters and morphological changes than earlier regimens</td>
</tr>
<tr>
<td>Prolongation of survival: Older patients are intrinsically at greater cardiovascular risk</td>
<td>ART reduces inflammatory markers and immune activation</td>
</tr>
<tr>
<td></td>
<td>HIV providers more aggressive about modification of ART or initiation of lipid-lowering therapies</td>
</tr>
</tbody>
</table>

### Predictors of Coronary Artery Stenosis 50% Among HIV-Infected ART-Treated Men

<table>
<thead>
<tr>
<th>Variable</th>
<th>Minimally Adjusted Risk §</th>
<th>Model Adjusted for CAD Risk Factors¶</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR (95% CI)</td>
<td>p-Value</td>
</tr>
<tr>
<td>Current HIV RNA level &gt; copies/mL</td>
<td>1.26 (0.76-2.10)</td>
<td>0.37</td>
</tr>
<tr>
<td>Duration of HAART use</td>
<td>1.09 (1.02-1.17)</td>
<td>0.007</td>
</tr>
<tr>
<td>History of AIDS</td>
<td>1.49 (0.92-2.41)</td>
<td>0.103</td>
</tr>
<tr>
<td>Current CD4+ T cell count</td>
<td>1.01 (0.93-1.09)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

§ Adjusted for age, race, CT scanning center and cohort before or after 2001.
¶Adjusted for age, race, CT scanning center, cohort, and CHD risk factors, SBP, antihypertensive medications, diabetes medication use, fasting glucose, total and HDL-C levels, use of lipid lowering agents, BMI and pack years of cigarette smoking.
Incidence of MI with Exposure to Combination Antiretroviral Therapy

The Incidence of MI per 1000 person-years for different levels of exposure to Combination Anti-Retroviral Therapy is shown in the graph. The data is provided by The Data collection on Adverse Events of Anti-HIV Drugs (DAD) Study Group.

The data collection on Adverse Events of Anti-HIV Drugs (DAD) Study Group*
Risk of MI with Exposure to NNRTIs

Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

- Delavirdine (DLV)
- Efavirenz (EFV)
- Etravirine (ETR)
- Nevirapine (NVP)
- Rilpivirine (RPV)
Risk of MI with Exposure to Protease Inhibitors

Protease Inhibitors

- Atazanavir (ATV)
- Darunavir (DRV)
- Fosamprenavir (FPV)
- Indinavir (IDV)
- Lopinavir/ritonavir (LPV/rKaletra) (boosting agent)
- Nelfinavir (NFV)
- Ritonavir (RTV) (used as a pharmacokinetic boosting agent)
- Saquinavir (SQV)
- Tipranavir (TPV)
CVD in HIV: Risk Factors in Post-ART Era

Cardiovascular Disease

Dyslipidemia
- ↑Triglycerides
- ↓HDL
- ↑Free Fatty Acids
- ↓↔LDL
- ↑Small Dense LDL

Insulin Resistance
- ↑ Glucose

Inflammation

Body Composition
- Lipoatrophy
- Lipohypertrophy

Insulin Resistance

HAART
- Specific ARV

Predisposing Factors
- Genetics, Smoking, Sedentary Lifestyle, Diet, Obesity, Hypertension & Renal Disease

Increased Mortality in HIV–Infected Subjects with High Baseline sCD14 Levels

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>&lt;25\textsuperscript{th} Percentile (Reference)</th>
<th>25\textsuperscript{th} – 49\textsuperscript{th} Percentile</th>
<th>50\textsuperscript{th} – 74\textsuperscript{th} Percentile</th>
<th>≥74\textsuperscript{th} Percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>sCD14 (×10\textsuperscript{5} pg/mL)</td>
<td>10/46</td>
<td>16/39</td>
<td>21/35</td>
<td>27/28</td>
</tr>
<tr>
<td>N (case patients/control subjects)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Univariate</td>
<td>1.0</td>
<td>2.1 (0.8–5.7)</td>
<td>.12</td>
<td>.01</td>
</tr>
<tr>
<td>Adjusted—risk factors(^{a})</td>
<td>1.0</td>
<td>2.8 (0.8–10.0)</td>
<td>.10</td>
<td>.11</td>
</tr>
</tbody>
</table>

\(^{a}\) Adjusted for age and baseline CD4+ T-cell count.

Sandler NG, et al. JID 2011;203:780-9
## Table 1: Association Between Inflammatory Macrophage Markers and Measures of Subclinical Carotid Artery Disease

<table>
<thead>
<tr>
<th></th>
<th>Any Carotid Artery Lesion</th>
<th>Distensibility ($10^{-6} \times N^{-1} \times m^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio</td>
<td>95% CI</td>
</tr>
<tr>
<td><strong>Individual inflammatory macrophage markers, per each standard deviation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Among entire study population (n=256)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gal-3BP</td>
<td>1.48*</td>
<td>1.01, 2.15</td>
</tr>
<tr>
<td>sCD163</td>
<td>1.85*</td>
<td>1.21, 2.83</td>
</tr>
<tr>
<td>sCD14</td>
<td>1.49*</td>
<td>1.04, 2.12</td>
</tr>
</tbody>
</table>

*Statistically significant at the p < 0.05 level.
Pathogenesis of Inflammation-Associated Disease in HIV-Infected Adults

Impact of HIV on Gut Mucosa

Impact of HIV on Inflammation, Coagulation, and Health

### Changes in Lipids and Lipoproteins After 24 Weeks of Antiretroviral Therapy

<table>
<thead>
<tr>
<th>Lipids, Lipoproteins</th>
<th>NRTIs + Efavirenz (PI-Sparing)</th>
<th>NRTIs + Lopinavir/ritonavir (NNRTI-Sparing)</th>
<th>Efavirenz + Lopinavir/ritonavir (NRTI-Sparing)</th>
<th>P&lt;sub&gt;KW&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total-C, mg/dL</td>
<td>18* (3 – 29)</td>
<td>21* (6 – 57)</td>
<td>65* (6 – 57)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>22 (-49 – 79)</td>
<td>72* (-1 – 186)</td>
<td>83* (11 – 164)</td>
<td>0.051</td>
</tr>
<tr>
<td>Direct LDL-C, mg/dL</td>
<td>6 (-5 – 24)</td>
<td>7 (-8 – 19)</td>
<td>26* (11 – 54)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL-C, mg/dL</td>
<td>9* (5 – 15)</td>
<td>3# (-1 – 13)</td>
<td>11* (7 – 17)</td>
<td>0.053</td>
</tr>
<tr>
<td>VLDL-P, nmol/L</td>
<td>13 (-16.6 – 33.4)</td>
<td>26.3* (2.8 – 60.3)</td>
<td>48.3* (14.2 – 84.4)</td>
<td></td>
</tr>
<tr>
<td>LDL-P, nmol/L</td>
<td>64 (-65 – 167)</td>
<td>135# (-115 – 312)</td>
<td>414* (120 – 740)</td>
<td>0.003</td>
</tr>
<tr>
<td>Small LDL-P, nmol/L</td>
<td>101 (-162 – 207)</td>
<td>127 (-162 – 357)</td>
<td>371 (-9 – 720)</td>
<td>0.039</td>
</tr>
<tr>
<td>HDL-P, μmol/L</td>
<td>5.3*</td>
<td>5.1*</td>
<td>8.3*</td>
<td>0.069</td>
</tr>
</tbody>
</table>

All values are medians (interquartile ranges) ; C (eg, LDL-C) = cholesterol, P (eg, LDL-P) = particle number
*p<0.01 compared to baseline, Wilcoxon signed rank probability test
#0.01≤p<0.05 compared to baseline, Wilcoxon signed rank probability test

Mechanisms for ART-Induced Lipoprotein Abnormalities

• Interference with ApoB proteasomal degradation

• Increased ApoC-III containing lipoproteins due to overproduction and impaired clearance

• Reduced lipoprotein lipase activity due to visceral adiposity (lipodystrophy), insulin resistance and acute phase response due to opportunistic infections
HIV Protease Inhibitor Protect ApoB Degradation by the Proteasome

PI treatment results in accumulation of cellular ApoB and ubiquitin-associated ApoB in HepG2 cells

Elevated LDL Particle Number in HIV-Infected Ethnic Minorities

- Participants recruited from a RCT of a dietary supplement to manage HIV-related dyslipidemia
- Cohort was 64% male; 92% African American

Lipoprotein (a) and HIV Disease Activity

Allele-specific apo(a) Levels for Smaller apo(a) sizes (<28 kringle [K] 4 repeats)

*P<0.001.

ApoC-III Triglyceride-Rich Lipoproteins are Elevated in HIV+ Men Treated with ART

Reduced HDL Functionality in HIV/ART

Inhibitory potency of each patient’s plasma needed to achieve 50% inhibition of hepatic CE uptake

## Drug Interactions – PI and Statins

<table>
<thead>
<tr>
<th>Drug</th>
<th>PI</th>
<th>Effect on PI on Statin Levels</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lovastatin</td>
<td>All</td>
<td>Significant ↑ Levels</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>All</td>
<td>Significant ↑ Levels</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>DRV/r</td>
<td>AUC ↑</td>
<td>Use lowest dose</td>
</tr>
<tr>
<td></td>
<td>LPV/r</td>
<td>AUC ↑</td>
<td>No adjustment</td>
</tr>
<tr>
<td></td>
<td>SQV/r</td>
<td>AUC ↓ 47-50%</td>
<td>No adjustment</td>
</tr>
<tr>
<td>Pitavastatin</td>
<td>All</td>
<td>AUC ↑ 31%</td>
<td>No adjustment</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>ATV/r</td>
<td>AUC ↑ 300%</td>
<td>Dosage ≤10 mg/d</td>
</tr>
<tr>
<td></td>
<td>LPV/r</td>
<td>AUC ↑ 108%, Cmax ↑ 366-700%</td>
<td>Dosage ≤10 mg/d</td>
</tr>
<tr>
<td></td>
<td>DRV/r</td>
<td>AUC ↑ 48%, Cmax ↑ 139%</td>
<td>Dosage ≤10 mg/d</td>
</tr>
</tbody>
</table>

## Drug Interactions – PIs and Statins

<table>
<thead>
<tr>
<th>Drug</th>
<th>PI</th>
<th>Effect on PI on Statin Levels</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin</td>
<td>ATV/r</td>
<td>↑ Levels</td>
<td>Lowest dosage</td>
</tr>
<tr>
<td></td>
<td>DRV/r</td>
<td>AUC ↑ 400%</td>
<td>Dosage ≤20 mg/d</td>
</tr>
<tr>
<td></td>
<td>FPV/r</td>
<td>AUC ↑ 400%</td>
<td>Dosage ≤20 mg/d</td>
</tr>
<tr>
<td></td>
<td>FPV</td>
<td>AUC ↑ 130-153%</td>
<td>Dosage ≤20 mg/d</td>
</tr>
<tr>
<td></td>
<td>SQV/r</td>
<td>AUC ↑ 79%</td>
<td>Dosage ≤20 mg/d</td>
</tr>
<tr>
<td></td>
<td>LPV/r</td>
<td>AUC ↑ 488%</td>
<td>Lowest dosage</td>
</tr>
<tr>
<td></td>
<td>TPV/r</td>
<td>AUC ↑ 836%</td>
<td>Do not use</td>
</tr>
</tbody>
</table>

# Drug Interactions – NNRTIs and Statins

<table>
<thead>
<tr>
<th>Drug</th>
<th>NNRTI</th>
<th>Effect on NNRTI on Statin Levels</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lovastatin</td>
<td>Efavirenz</td>
<td>Significant ↑ levels</td>
<td>Contraindicated</td>
</tr>
<tr>
<td></td>
<td>Etravirine</td>
<td>↓ lovastatin levels</td>
<td>---</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>Nevirapine</td>
<td>↓ simvastatin levels</td>
<td>---</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>Efavirenz</td>
<td>AUC ↓ 44%</td>
<td>Adjustment based on lipid levels</td>
</tr>
<tr>
<td></td>
<td>Etravirine</td>
<td>No significant effect</td>
<td>No adjustment</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>Etravirine</td>
<td>↑ Fluvastatin possible</td>
<td>Cautious use</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>Etravirine</td>
<td>No significant effect</td>
<td>No adjustment</td>
</tr>
<tr>
<td>Pitavastatin</td>
<td>Efavirenz</td>
<td>No data</td>
<td>No recommendation</td>
</tr>
<tr>
<td></td>
<td>Etravirine</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nevirapine</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rilpivirine</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fixed Combination ARTs

- Abacavir-lamivudine (ABC/3TC)
- Abacavir-lamivudine-zidovudine (ABC/3TC/ZDV) Trizivir
- Efavirenz-tenofovir-emtricitabine (EFV/TDF/FTC)
- Elvitegravir-cobicistat-tenofovir-emtricitabine (EVG/COBI/TDF/FTC)
- Tenofovir-emtricitabine (TDF/FTC)
- Rilpivirine-emtricitabine-tenofovir (RPV/FTC/TDF)
- Zidovudine-lamivudine (ZDV/3TC)
# Lipid Changes in Comparator Studies of 3 Commonly Used ART Therapies

<table>
<thead>
<tr>
<th></th>
<th>Elvitegavi, Cobicstat, Emtricitabine Tenofovir (N=701)</th>
<th>Efavirenz/Emtricitabine/Tenofovir (N=352)</th>
<th>ATV + RTV + Emtricitabine/Tenofovir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>Wk 96</td>
<td>Baseline</td>
<td>Wk 96</td>
</tr>
<tr>
<td>mg/dL</td>
<td>% Change</td>
<td>mg/dL</td>
<td>% Change</td>
</tr>
<tr>
<td>TC</td>
<td>166</td>
<td>+12</td>
<td>161</td>
</tr>
<tr>
<td>LDL-C</td>
<td>100</td>
<td>+12</td>
<td>97</td>
</tr>
<tr>
<td>HDL-C</td>
<td>43</td>
<td>+7</td>
<td>43</td>
</tr>
<tr>
<td>TG</td>
<td>122</td>
<td>+8</td>
<td>121</td>
</tr>
</tbody>
</table>

Product circular
Commonly Used Combination ART and Interactions with Statins

- Emtricitabine/tenofovir
  - No reported interactions

- Efavirenz/emtricitabine/tenofovir
  - Simvastatin ↓ AUC 68% (62-73)
  - Atorvastatin ↓ AUC 43% (34-50)
  - Pravastatin ↓ AUC 44% (26-57)

- Elvitegravir, cobicstat, emtricitabine, tenofovir
  - Lovastatin, Simvastatin (contraindication)
  - Atorvastatin ↑ levels (start lowest dose, titrate carefully)
  - Rosuvastatin – No interaction

Ref – Product circulars
HIV-Infected Individuals: Mean Percent Change from Baseline to Week 52 in LDL-C, ApoB, non-HDL-C (INTREPID)

**LDL-C**
- Pitavastatin 4mg: -29.7 (17.4)
- Pravastatin 40mg: -20.5 (15.4)

Mean % Change (SD) in Apolipoprotein B
- Pitavastatin 4mg: -25.4 (13.8)
- Pravastatin 40mg: -19.6 (13.4)

Mean % Change (SD) in non-HDL-C
- Pitavastatin 4mg: -26.1 (15.9)
- Pravastatin 40mg: -19.0 (14.5)

Difference in LS Mean %Δ:
- LDL-C: -8.4, P<0.001
- ApoB: -4.9, P<0.001
- non-HDL-C: -5.7, P<0.001

Sponsors CA, et al. CROI 2014, poster presented
### INTREPID: Change from Week 0 to 52 in HIV-1 RNA Viral Load, CD4 Cell Count, and hs-CRP

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pitavastatin 4 mg (n=98)</th>
<th>Pravastatin 40 mg (n=90)</th>
<th>P-value&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1 RNA viral load, log copies&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.03 (0.4)</td>
<td>0.07 (0.4)</td>
<td>0.81</td>
</tr>
<tr>
<td>CD4 count, cells/mm&lt;sup&gt;3&lt;/sup&gt;</td>
<td>-8.3 (124.0)</td>
<td>36.5 (157.5)</td>
<td>0.18</td>
</tr>
<tr>
<td>hsCRP, mg/L</td>
<td>-1.2 (6.5)</td>
<td>-1.1 (14.4)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

<sup>a</sup>n= 97 for pitavastatin  
<sup>b</sup>p-values from ANCOVA model of LS mean percent change from baseline  
Sponseller CA, et al. CROI 2014, poster presented
REPRIEVE Trial

- NIH initiated multi-center randomized, placebo-controlled trial of pitavastatin 4 mg daily to prevent CVD events in HIV-infected individuals ≥40 years of age with LDL-C <130 mg/dL
- 6,500 individuals who have no current indication for a statin
- Thus, exclusions include patients with established atherosclerotic CVD and diabetes.
- Primary endpoint: Major adverse cardiovascular events (MACE)
- Follow-up 5 years
HIV Infection As A Chronic Disease

Continuum of chronic HIV disease

HIV infection

Antiretroviral treatment (inhibition of HIV replication)

Immune dysfunction/inflammation (lymphoid fibrosis, cytomegalovirus, copathogens, microbial translocation, HIV)

Treatment toxicity (metabolic syndrome, kidney dysfunction, liver dysfunction, neuropathy)

Non-AIDS morbidity (coronary artery disease, osteoporosis, cancer)

Geriatric syndromes/ageing (sarcopenia, frailty)

Overburdened health-care delivery systems

Interventions

Testing, linkage to care, retention in care

Less toxic ART

Anti-inflammatory and immune-boosting drugs

Aggressive preventive medicine (lipid and blood pressure management, cancer screening)

Healthy ageing (exercise, diet)

Operations research (chronic-care model)

Conclusions

• ART therapy has changed HIV-infection into a chronic illness characterized by high rates of atherosclerotic CVD disease

• The major contributing causes of CVD in ART-treated HIV patients includes inflammation, overproduction of apoB-containing lipoproteins, dysfunctional HDL and insulin resistance

• Risk reduction with statins is complicated by statin associated adverse muscle events with NNRTIs and drug interactions with PIs.

• Newer apoB-lowering therapies may be important in reducing residual risk in statin-ART treated HIV patients.