Cardiovascular Disease and HIV

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Efficacy of Newer Antiretroviral Therapy

Year of study commencement

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Efficacy (SD)</td>
<td>47% (14)</td>
<td>52% (17)</td>
<td>64% (7.1)</td>
<td>74% (8.5)</td>
<td>82% (6.7)</td>
</tr>
</tbody>
</table>
Potential Survival Gain after ART Initiation in A High Income Country

Expected survival of a 20-year-old person living with HIV in a high income country

Life Expectancy after Initiation of Combination Antiretroviral Therapy in Thailand

Expected survival of a 20-year-old person living with HIV in a middle income country

• To estimate the expected additional years of life in HIV-infected Thai people after starting ART through the National AIDS Program (NAP)
• Patients aged ≥15 years at ART initiation between 2008 and 2014
• 201,688 patients contributing 618,837 person-years of follow-up
• Median CD4 109 cells/mm$^3$
• Median age 37 years

Era of ART

+53.2  +60.0

+33.6  +47.0

years

HIV+
2008-2014

HIV-negative
Changing Patterns of the Causes of Death

Causes of Death in Participants in the Swiss HIV Cohort Study in 3 Different Time Periods, and in the Swiss Population in 2007

Yrs of Death of HIV-Positive Persons vs Swiss Population

Significant Mortality of CVD in HIV-infected Patients

- 1,876 deaths among 39,727 patients
- Non-AIDS related deaths accounted for 50.5%
- ~16% were due to CVD

Trends in Causes of Death in People with HIV from 1999 to 2011 (D:A:D)

- A collaboration of 11 cohort studies at 212 clinics in Europe, USA, and Australia
- 3,909 of 49,731 patients died during 308,719 person-years of follow-up

- AIDS-related (29%)
- Non-AIDS cancer (15%)
- Liver-related (13%)
- CVD-related (11%)
  - Myocardial infarction (6%)
  - Stroke (1%)
  - Other CVD (2%)
  - Other heart disease (2%)
  - Complications due to diabetes (<0.5%)
- Others or unknown (32%)

HIV and Cardiovascular Diseases (CVD)

- Rate of acute MI higher in HIV-positive patients
- HIV infection is a risk factor for ischemic stroke
- HIV-infected men have a greater prevalence of coronary artery plaque

Cohorts (HIV +ve = 3851, HIV -ve = 1,044,589) were identified in the Research Patient Data Registry

Primary outcome was AMI.

Cardiovascular Risk Factors in HIV

5. NICE CVD Guidelines 2014.
6. CKD in Adults: UK Guidelines
8. Klein D et al. 18th CROI, 2011; Abstract 810.
10. WHO CVD Guidelines.
Pathogenesis and Risk Factors of CVD in HIV

1. Traditional risk factors:
   – Higher prevalence of conventional risk factors for CVD in HIV
     • Smoking, hypertension, diabetes mellitus, and dyslipidemia

2. HIV infection:
   – Relative risk of CVD was 1.61 among HIV-infected patients without ART compared to HIV-uninfected
   – HIV infection is associated with premature development of CVD
     • Impaired lipid metabolism, inflammation, or endothelial function
     • Persistent HIV viremia and immunosuppression

3. Antiretroviral therapy:
   – Some drugs, esp. PIs, are associated with dyslipidemia
   – Specific drugs are associated with CVD e.g. PI?, ABC?, ddI?
Traditional Risk Factors in HIV-infected Patients

Retrospective, healthcare system based observational study. N = 3,851 HIV+ patients and 1,044,589 non-HIV patients

![Graph showing rates of hypertension, diabetes, and dyslipidemia in HIV-positive vs. HIV-negative patients.](https://example.com/graph.png)

- Hypertension: HIV positive: 21.2, HIV negative: 15.9
- Diabetes: HIV positive: 11.5, HIV negative: 6.6
- Dyslipidemia: HIV positive: 23.3, HIV negative: 17.6

*p < .0001 for all comparisons

HIV positive vs HIV negative

Reducing CVD Risk Factors can Decrease CVD in Older HIV-infected Patients

- Effective treatment of modifiable risk factors, such as smoking, cholesterol, and BP can significantly reduce an individual’s CVD risk.

Model for Change in Relative Risk of CVD From Smoking Cessation, Reducing Cholesterol,* or Reducing Systolic BP† in a Cohort of 24,323 HIV-Positive Pts Without Prior CVD (DAD Study)

*Reduced by 1 mmol/L. †Reduced by 10 mm Hg.

Pathogenesis and Risk Factors of CVD in HIV

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Currier JS. Circulation 2008; 118:e29-35.
HIV Patients Have Chronic Immune Activation

Percentage difference in the levels of hsCRP, IL-6, D-dimer and cystatin C in HIV-infected study participants 45-76 years of age versus the general population

- Persistent inflammation is observed in HIV infection
- Inflammatory markers linked to CVD disease in general population (high sensitivity C-reactive protein [hsCRP], interleukin-6 [IL-6] and D-dimer associated with all-cause mortality are higher in HIV-infected patients

Patients with sustained viral suppression had lower levels of T-cell activation than untreated patients but higher levels than uninfected controls. These T-cell activations contribute to some of the chronic inflammatory response.

Markers Associated with CVD Risk

D-dimer and sVCAM associated with Increased Risk for CVD

- Case controlled study of CVD events - 52 of 1892 patients since 1995
- Significant traditional risk factors for events: smoking, family history, lipids
- Conclusions: Biomarkers may help stratify CVD risk in HIV patients

### Low CD4 Cell Counts as Risk Factors of Primary MI

<table>
<thead>
<tr>
<th>Model</th>
<th>Adjusted Risk of Primary MI*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unweighted CD4 models</strong></td>
<td></td>
</tr>
<tr>
<td>CD4 &lt; 100</td>
<td>1.95 (1.13-3.36)</td>
</tr>
<tr>
<td>CD4 &lt; 200</td>
<td>1.69 (1.07-2.67)</td>
</tr>
<tr>
<td>CD4 &lt; 350</td>
<td>1.36 (0.88-2.08)</td>
</tr>
<tr>
<td>CD4 &lt; 500</td>
<td>1.26 (0.79-2.01)</td>
</tr>
<tr>
<td><strong>CD4 and HIV-1 RNA models (reference: ≥ threshold and undetectable HIV-1 RNA)</strong></td>
<td></td>
</tr>
<tr>
<td>CD4 ≥ 350 and detectable HIV-1 RNA</td>
<td>1.81 (1.17-2.81)</td>
</tr>
<tr>
<td>CD4 ≥ 500 and detectable HIV-1 RNA</td>
<td>1.61 (1.03-2.54)</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex, tobacco, IDU, MSM, diabetes, statin use, treated hypertension, eGFR, ART.

- Traditional CVD risk factors are important predictors of primary MIs
- Low CD4+ cell count independently predicts primary MIs
- Detectable HIV-1 RNA associated with primary MI risk at CD4+ cell counts ≥ 350 and ≥ 500 cells/mm³
Pathogenesis and Risk Factors of CVD in HIV

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   - Some drugs, esp. PIs, are associated with dyslipidemia
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Currier JS. Circulation 2008; 118:e29-35.
Median TC and TG Change From Baseline in Comparative Studies of RTV-Boosted PIs

- TC (mmol/L)
- TG (mmol/L)

Bar chart showing the comparison of Median TC and TG Change From Baseline in various studies:

- CASTLE
- ARTEMIS
- GEMINI
- KLEAN
Atazanavir/ritonavir (ATV/r) vs Efavirenz (EFV) in Treatment-naïve Patients (ACTG 5202)

- Randomized, noninferiority phase III studies
- Primary endpoint: HIV-1 RNA < 50 copies/mL at week 48

**ACTG 5202**
(third agent, open label)

**ART-naive pts**
VL ≥ 1000 c/mL (N = 1857)

**TDF/FTC + EFV** (n = 464)
**TDF/FTC + ATV/r** (n = 465)
**ABC/3TC + EFV** (n = 465)
**ABC/3TC + ATV/r** (n = 463)

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**ACTG 5202**

<table>
<thead>
<tr>
<th>Variable</th>
<th>TDF/FTC + EFV</th>
<th>TDF/FTC + ATV/r</th>
<th>ABC/3TC + EFV</th>
<th>ABC/3TC + ATV/r</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC</td>
<td>P &lt; .001</td>
<td>P = .002</td>
<td>P &lt; .001</td>
<td>P &lt; .001</td>
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<tr>
<td>LDL</td>
<td>22</td>
<td>21</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>HDL</td>
<td>10</td>
<td>13</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>TG</td>
<td>24</td>
<td>14</td>
<td>15</td>
<td>13</td>
</tr>
</tbody>
</table>

## Abacavir Use and Myocardial Infarction

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients</th>
<th>Design</th>
<th>Myocardial infarction (MI) events</th>
<th>Effect of ABC (on MI event)?</th>
</tr>
</thead>
<tbody>
<tr>
<td>D:A:D cohort¹</td>
<td>33,347</td>
<td>Observational cohort</td>
<td>Prospective, predefined</td>
<td>Yes</td>
</tr>
<tr>
<td>FHDH²</td>
<td>1,173</td>
<td>Nested case control study</td>
<td>Prospective, MI retrospectively validated</td>
<td>No*</td>
</tr>
<tr>
<td>VA cohort³,⁴</td>
<td>19,424</td>
<td>Observational cohort</td>
<td>Prospective, predefined</td>
<td>No†</td>
</tr>
<tr>
<td>ACTG cohort (A2001/ALLRT)⁵</td>
<td>5,055</td>
<td>Observational cohort</td>
<td>Prospective, predefined</td>
<td>No</td>
</tr>
</tbody>
</table>

All or majority of patients antiretroviral experienced at ABC initiation

*Short-term/recent exposure to ABC (<1 year) was associated with an increased risk of MI; however, the association disappeared when the analysis was restricted to non-users of cocaine and intravenous drugs
†No association found after adjustment for chronic kidney disease, drug use, history of smoking, etc.

1. Lundgren JD et al. 16th CROI 2009. Abstract 44LB.
FDA Meta-analysis: No Association between Abacavir Use and Myocardial Infarction

- Retrospective review of 26 randomized controlled clinical trials (N=9868)
- Largest trial-level meta-analysis to date of clinical trials in which ABC use was randomized
- 5028 ABC patients and 4840 non-ABC patients
- 24 MI events in 5028 ABC patients vs 22 MI events in 4840 no-ABC patients
When selecting a regimen for an individual patient, a number of patients and regimen specific characteristic should be considered, with the goal of providing a potent, safe, tolerable, and easy to adhere to regimen for the patient *in order to achieve sustained virologic control*. 

- CVD is one of several specific comorbidities listed among those to consider.
- In patients with high cardiac risk, consider avoiding ABC-containing regimens.

  • Associated with increased cardiovascular risk in some studies.

DHHS Guidelines: Factors to Consider When Selecting an Initial ART Regimen

DHHS Adult Guidelines. April 2015.
Potential Clinical Impact of Lipodystrophy

- **Morphological**
  - Quality of life
  - Patient adherence

- **Metabolic**
  - Insulin resistance
  - Impaired glucose tolerance
  - Type 2 diabetes
  - Hypertriglyceridemia
  - Hypercholesterolemia
  - Increased free fatty acids (FFA)
  - Decreased high density lipoprotein (HDL)

- **Psychological**
  - Depression
  - Social discrimination

Pathogenesis and Risk Factors

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     • Persistent HIV viremia and immunosuppression

3. Antiretroviral therapy:
   – Some drugs, esp. PIs, are associated with dyslipidemia
   – Specific drugs are associated with CVD e.g. PI?, ABC?, ddi?

Currier JS. Circulation 2008; 118:e29-35.
Absolute rates of MI and stroke have declined with

- CVD risk factor reduction
- Improvements in immune status
- Use of ART regimens with better lipid effects


Management of Dyslipidemia in HIV-infected Patients Receiving Antiretroviral Therapy

2 Strategies to manage dyslipidemia

Switching Strategy
Switching ART to a more lipid-friendly regimen while maintain complete viral suppression

Adding Strategy
Adding lipid-lowering agent to current ART regimen
# Antiretroviral Agents and Availability in Thailand

<table>
<thead>
<tr>
<th>NRTIs</th>
<th>NNRTIs</th>
<th>PIs</th>
<th>INIs</th>
<th>FI &amp; EI</th>
<th>Combined</th>
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</thead>
<tbody>
<tr>
<td>AZT</td>
<td>EFV</td>
<td>IDV</td>
<td>RAL</td>
<td>T-20</td>
<td>AZT/3TC</td>
</tr>
<tr>
<td>d4T</td>
<td>NVP</td>
<td>LPV</td>
<td>EVG</td>
<td>MRV</td>
<td>TDF/FTC</td>
</tr>
<tr>
<td>ddI</td>
<td>RPV</td>
<td>ATV</td>
<td>DTG</td>
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<td>ABC/3TC</td>
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<tr>
<td>3TC</td>
<td>ETR</td>
<td>SQV</td>
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<td>TDF/FTC/EFV</td>
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<td>FTC</td>
<td></td>
<td>FPV</td>
<td></td>
<td></td>
<td>TDF/FTC/RPV</td>
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<tr>
<td>TDF</td>
<td></td>
<td>DRV</td>
<td></td>
<td></td>
<td>TDF/FTC/EVG/COBI</td>
</tr>
<tr>
<td>ABC</td>
<td></td>
<td>TPV</td>
<td></td>
<td></td>
<td>ABC/3TC/DTG</td>
</tr>
</tbody>
</table>

*Updated 31 MAY 2017*
Number of HIV-infected Patients Registered in Thai National AIDS Program (NAP) and NAP Budget

- **Budget**: Million USD
- **Number of patients**: 64,422
- **128.5**
- **94,842**
- **146.1**
- **116,416**
- **131,152**
- **149,910**
- **162,440**
- **174,400**

- **Increasing Number of Patients**
- **Non-variable Budget**

www.nhso.go.th
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

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

# Use of Statins in HIV-infected Patients

## Drugs used to lower LDL-c

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Drug</th>
<th>Dose</th>
<th>Side effects</th>
<th>Advise on use of statin together with ART use with PI/r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statin</td>
<td>atorvastatin</td>
<td>10-80 mg qd</td>
<td>Gastrointestinal symptoms, headache, insomnia, rhabdomyolysis (rare) and toxic hepatitis</td>
<td><strong>Start with low dose</strong> (max: 40 mg)</td>
</tr>
<tr>
<td></td>
<td>fluvastatin</td>
<td>20-80 mg qd</td>
<td></td>
<td>Consider higher dose</td>
</tr>
<tr>
<td></td>
<td>pravastatin</td>
<td>20-80 mg qd</td>
<td></td>
<td>Consider higher dose</td>
</tr>
<tr>
<td></td>
<td>rosuvastatin</td>
<td>5-40 mg qd</td>
<td></td>
<td><strong>Start with low dose</strong> (max: 20 mg)</td>
</tr>
<tr>
<td></td>
<td>simvastatin</td>
<td>10-40 mg qd</td>
<td></td>
<td>Start with low dose</td>
</tr>
<tr>
<td>Intestinal cholesterol</td>
<td>ezetimibe</td>
<td>10 mg qd</td>
<td>Gastrointestinal symptoms</td>
<td>Contra-indicated</td>
</tr>
<tr>
<td>absorption inhibitor</td>
<td></td>
<td></td>
<td></td>
<td>No known drug-drug interactions with ART</td>
</tr>
</tbody>
</table>

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**Notes:**

- A statin is preferred first-line therapy; different statins have variable intrinsic LDL-c lowering ability.
- Target levels for LDL-c, see page 36. In persons where LDL-c targets are difficult to achieve, consult/refer to specialist.
- Expected range of reductions of LDL-c: i 1.5-2.5 mmol/L (60-100 mg/dL), ii 0.8-1.5 mmol/L (35-60 mg/dL), iv 0.2-0.5 mmol/L (10-20 mg/dL).
- The ARV may inhibit (statin toxicity, ↓ dose) or induce (=less effect of statin, ↑ dose gradually to achieve expected benefit) the excretion of the statin.
- Exception: If used with DRV/r, start with lower dose of pravastatin.
- This agent can be used for HIV-positive persons intolerant of statins or added to a statin when LDL reduction is inadequate despite maximally tolerated statin.
- Pitavastatin has as yet no morbidity/mortality trial data to support its use but may have advantages of fewer drug-drug interactions, more HDL increase and less adverse glucose effect than other statins.

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HIV-infected Patients Receiving LPV/r as A Component of Second-line ART and Dyslipidemia

2 Strategies to manage dyslipidemia

Switching strategy
Changing LPV/r → ATV/r or DRV/r

Adding strategy
LPV/r + lipid-lowering agent

Switching strategy
Changing LPV/r → ATV/r

Adding strategy
LPV/r + Atorvastatin 20 mg

LPV/r = Lopinavir/ritonavir
ATV/r = Atazanavir/ritonavir
Switching Lopinavir/Ritonavir to Atazanavir/Ritonavir vs Adding Atorvastatin in HIV-Infected Patients Receiving Second-Line Antiretroviral Therapy With Hypercholesterolemia: A Randomized Controlled Trial

Phanthaboon Wangpatharawanit and Somnuek Sungkanuparph

Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand
Mean change in lipid profile between switching group and adding group at 12, 24, 36, and 48 weeks

**Week 12**

<table>
<thead>
<tr>
<th></th>
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<th>2</th>
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<th>4</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Reeks1</td>
<td>-14,5</td>
<td>-1,6</td>
<td>0,7</td>
<td>-92,7</td>
<td>0,013</td>
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<tr>
<td>Reeks2</td>
<td>-47,4</td>
<td>-28,7</td>
<td>-1,2</td>
<td>-50,7</td>
<td>0,357</td>
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**Week 24**

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<tbody>
<tr>
<td>Reeks1</td>
<td>-16,7</td>
<td>2,6</td>
<td>1,6</td>
<td>-102,3</td>
<td>0,003</td>
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<tr>
<td>Reeks2</td>
<td>-52,8</td>
<td>-31,6</td>
<td>-1,5</td>
<td>-72,5</td>
<td>0,257</td>
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</tbody>
</table>

**Week 36**

<table>
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</thead>
<tbody>
<tr>
<td>Reeks1</td>
<td>-22,4</td>
<td>-3,8</td>
<td>2,5</td>
<td>-88,6</td>
<td>0,056</td>
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<tr>
<td>Reeks2</td>
<td>-58,1</td>
<td>-41,1</td>
<td>-4,4</td>
<td>-64,9</td>
<td>0,001</td>
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**Week 48**

<table>
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<tr>
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<th>3</th>
<th>4</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reeks1</td>
<td>-19,1</td>
<td>1,2</td>
<td>1,2</td>
<td>-89,1</td>
<td>0,010</td>
</tr>
<tr>
<td>Reeks2</td>
<td>-51,8</td>
<td>-28,7</td>
<td>-0,7</td>
<td>-71,1</td>
<td>0,696</td>
</tr>
</tbody>
</table>
Randomized Trial of Statin Therapy and Coronary Plaque Progression

- Randomized 12-month trial in HIV-infected patients on stable ART with LDL < 130 and ≥ 1 coronary plaque
  - Atorvastatin 20 mg (↑ to 40 mg at 3 months) (n=19) vs Placebo (n=21)
- Statin therapy reduced progression of coronary plaques
  - Reduced overall plaque volume, including lipid-laden plaques
  - Reduced high-risk morphology plaques
- Statin therapy safe and well tolerated


Plaque Progression in Proximal Left Anterior Descending Coronary Artery With Atorvastatin or Placebo

Baseline

12 months

Atorvastatin

Placebo
2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults

Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, American Pharmacists Association, American Society for Preventive Cardiology, Association of Black Cardiologists, Preventive Cardiovascular Nurses Association, and Women Heart: The National Coalition for Women with Heart Disease

© American College of Cardiology Foundation and American Heart Association, Inc.
4 Statin Benefit Groups

✓ Clinical ASCVD*
✓ LDL-C ≥190 mg/dL, Age ≥21 years
✓ Diabetes: Age 40-75 years, LDL-C 70-189 mg/dL
✓ No Diabetes‡: ≥7.5%‡ 10-year ASCVD risk, Age 40-75 years, LDL-C 70-189 mg/dL

- Statin therapy should be based on the degree of ASCVD risk and the intensity of the statin
- Not recommend for or against LDL-C targets

*Atherosclerotic cardiovascular disease
†Requires risk discussion between clinician and patient before statin initiation
‡Statin therapy may be considered if risk decision is uncertain after use of ASCVD risk calculator

Individual responses to statin therapy varied in the RCTs and should be expected to vary in clinical practice. There might be a biologic basis for a less-than-average response.

†Evidence from 1 RCT only: down-titration if unable to tolerate atorvastatin 80 mg in IDEAL (Pedersen et al).
‡Although simvastatin 80 mg was evaluated in RCTs, initiation of simvastatin 80 mg or titration to 80 mg is not recommended by the FDA due to the increased risk of myopathy, including rhabdomyolysis.

### Intensity of Statin Therapy

<table>
<thead>
<tr>
<th>High-Intensity Statin Therapy</th>
<th>Moderate-Intensity Statin Therapy</th>
<th>Low-Intensity Statin Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily dose lowers LDL–C on average, by approximately ≥50%</td>
<td>Daily dose lowers LDL–C on average, by approximately 30% to &lt;50%</td>
<td>Daily dose lowers LDL–C on average, by &lt;30%</td>
</tr>
</tbody>
</table>

**Atorvastatin (40†)–80 mg**

**Rosuvastatin 20 (40) mg**

**Atorvastatin 10 (20) mg**

**Rosuvastatin (5) 10 mg**

**Simvastatin 20–40 mg‡**

**Pravastatin 40 (80) mg**

**Lovastatin 40 mg**

**Fluvastatin XL 80 mg**

**Fluvastatin 40 mg bid**

**Pitavastatin 2–4 mg**

**Simvastatin 10 mg**

**Pravastatin 10–20 mg**

**Lovastatin 20 mg**

**Fluvastatin 20–40 mg**

**Pitavastatin 1 mg**

*Individual responses to statin therapy varied in the RCTs and should be expected to vary in clinical practice. There might be a biologic basis for a less-than-average response.

†Evidence from 1 RCT only: down-titration if unable to tolerate atorvastatin 80 mg in IDEAL (Pedersen et al).
‡Although simvastatin 80 mg was evaluated in RCTs, initiation of simvastatin 80 mg or titration to 80 mg is not recommended by the FDA due to the increased risk of myopathy, including rhabdomyolysis.*
Summary

• Current ART significantly improve survival of HIV-infected patients

• There are changing patterns of the causes of death
  – Non-AIDS events esp. heart, liver, kidney, bone diseases are increasing
  – Rates of CVD in HIV-infected patients higher than general population

• Pathogenesis and risk factors of CVD
  – Traditional risk factors for CVD
  – HIV infection itself
  – Antiretroviral therapy

• Management of CVD in HIV
  – Starting ART early can decrease CVD risk
  – Practical management in each setting may be different
  – Prevention is the key
  – Screening and monitoring the CVD risk with primary prevention
Heart-healthy lifestyle habits are the foundation of ASCVD prevention (See 2013 AHA/ACC Lifestyle Management Guideline)

Age ≥ 21 y and a candidate for statin therapy

Clinical ASCVD

Age ≤ 75 y
High-intensity statin
(Moderate-intensity statin if not candidate for high-intensity statin)

Age > 75 y OR if not candidate for high-intensity statin
Moderate-intensity statin

LDL-C ≥ 190 mg/dL

High-intensity statin
(Moderate-intensity statin if not candidate for high-intensity statin)

LDL-C 70-189 mg/dL
Age 40-75 y

Diabetes

Moderate-intensity statin

Estimated 10-y ASCVD risk ≥ 7.5%†
High-intensity statin

Definitions of High- and Moderate-Intensity Statin Therapy* (See Table 5)

High
Daily dose lowers LDL-C by approx. ≥ 50%

Moderate
Daily dose lowers LDL-C by approx. 30% to < 50%

Regularly monitor adherence to lifestyle and drug therapy with lipid and safety assessments (See Fig 5)

Primary prevention
(No diabetes, LDL-C 70 to 189 mg/dL, and not receiving statin therapy)

Estimate 10-y ASCVD risk every 4-6 y using Pooled Cohort Equations†

DM age <40 or >75 y or LDL-C <70 mg/dL

- <5% 10-y ASCVD risk‡
- Age <40 or >75 y and LDL-C <190 mg/dL‡
- ≥7.5% 10-y ASCVD risk (Moderate- or high-intensity statin)
- 5% to <7.5% 10-y ASCVD risk (Moderate-intensity statin)

In selected individuals, additional factors may be considered to inform treatment decision making§

Clinician-Patient Discussion
Prior to initiating statin therapy, discuss:
1. Potential for ASCVD risk-reduction benefits ||
2. Potential for adverse effects and drug–drug interactions‡‡
3. Heart-healthy lifestyle
4. Management of other risk factors
5. Patient preferences
6. If decision is unclear, consider primary LDL-C ≥160 mg/dL, family history of premature ASCVD, lifetime ASCVD risk, abnormal CAC score or ABI, or hs-CRP ≥2 mg/L§

Emphasize adherence to lifestyle
Manage other risk factors
Monitor adherence

Yes to statin

Encourage adherence to lifestyle
Initiate statin at appropriate intensity
Manage other risk factors
Monitor adherence* (See Fig 5)

No to statin

SATURN-HIV: double-blind, randomized, placebo-controlled trial of rosvuastatin in HIV-infected patients (N = 147)

CAC, coronary artery calcium; CCA, common carotid artery; CIMT, carotid intima-media thickness