2015 HIV Update

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Disclosures

• I have no financial relationships to disclose.

• I will not discuss off-label use and/or investigational use in my presentation.

• Slides provided by various sources including AETC, CDC, DHHS, and Dr. Paul Sax.
• 1.2 million adults and adolescents are living with HIV in the United States

• Approximately 602,000 persons diagnosed with AIDS have died in the US

• 50,000 people are newly infected each year in the US

• The proportion of persons with HIV who know they are infected increased from 75% in 2003 to 80% in 2008
Arizona

- Prevalence of reported HIV/AIDS infection is 230 cases per 100,000 persons

- Increased population growth may be contributing to an increase in prevalence

- As of December 31, 2011, there were 14,705 people reported living with HIV/AIDS in Arizona

<table>
<thead>
<tr>
<th>Population</th>
<th>New HIV Infections (Number)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Women</td>
<td>9853</td>
</tr>
<tr>
<td>Black Women</td>
<td>12,069</td>
</tr>
<tr>
<td>Hispanic Women</td>
<td>7199</td>
</tr>
<tr>
<td>Black Men</td>
<td>5268</td>
</tr>
<tr>
<td>White Men</td>
<td>2493</td>
</tr>
<tr>
<td>Black Female</td>
<td>1174</td>
</tr>
<tr>
<td>Hispanic Male</td>
<td>1232</td>
</tr>
<tr>
<td>Black Male</td>
<td>903</td>
</tr>
<tr>
<td>Hispanic Female</td>
<td>532</td>
</tr>
</tbody>
</table>

Total Estimated New HIV Infections in 2013 (n=47,352)

Disease progress is influenced by viral characteristics and individual host factors.

**Early Symptoms**
- Generalized lymphadenopathy
- Oral hairy leukoplakia
- Diffuse histiocytic lymphoma
- Dermatologic changes (herpes zoster, tuberculosis)

**Opportunistic Infections**
- Bacterial, viral, fungal, parasitic infections

**Neoplastic Diseases**
- Kaposi's sarcoma, lymphoma, invasive cervical cancer

**Neurologic Manifestations**
- Dementia; changes in gait, concentration, memory, affect; peripheral neuropathy

After the primary infection period, a higher viral burden predicts more rapid disease progression and a higher risk of transmission from pregnant women to offspring.

Wasting, opportunistic infections, neoplastic diseases, and neurologic manifestations occur more frequently in late HIV/AIDS and may become chronic.
All of the following are key target sites for HIV Antiretroviral therapy except?

A. Reverse Transcriptase
B. Integrase
C. Protease
D. DNA Polymerase
E. CCR5
Current Antiretroviral (ART) Medications

NRTI/NTRTI
- Abacavir (ABC)
- Didanosine (ddI)
- Emtricitabine (FTC)
- Lamivudine (3TC)
- Stavudine (d4T)
- Tenofovir (TDF) NT
- Zidovudine (AZT, ZDV)

NNRTI
- Delavirdine (DLV)
- Efavirenz (EFV)
- Etravirine (ETR)
- Nevirapine (NVP)
- Rilpivirine (RPV)

Protease Inhibitors
- Atazanavir (ATV)
- Darunavir (DRV)
- Fosamprenavir (FPV)
- Indinavir (IDV)
- Lopinavir (LPV)
- Nelfinavir (NFV)
- Ritonavir (RTV)
- Saquinavir (SQV)
- Tipranavir (TPV)

Integrase Inhibitor
- Raltegravir (RAL)
- Elvitegravir (EVG)
- Dolutegravir (DTG)

Fusion Inhibitor
- Enfuvirtide (ENF, T-20)

CCR5 Antagonist
- Maraviroc (MVC)

Combinations
- Atripla
- Complera
- Stribild
- Triumeq
FIGURE 3. Number and percentage of HIV-infected persons engaged in selected stages of the continuum of HIV care — United States

<table>
<thead>
<tr>
<th>Engagement in HIV care</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-infected*</td>
<td>1,178,350</td>
<td>100%</td>
</tr>
<tr>
<td>HIV-diagnosed*</td>
<td>941,950</td>
<td>81%</td>
</tr>
<tr>
<td>Linked to HIV care†</td>
<td>725,302</td>
<td>62%</td>
</tr>
<tr>
<td>Retained in HIV care§</td>
<td>480,395</td>
<td>41%</td>
</tr>
<tr>
<td>On ART§</td>
<td>426,590</td>
<td>36%</td>
</tr>
<tr>
<td>Suppressed viral load (≤200 copies/mL)**</td>
<td>328,475</td>
<td>28%</td>
</tr>
</tbody>
</table>

Abbreviations: HIV = human immunodeficiency virus; ART = antiretroviral therapy.

In November 2012, the U.S. Preventive Services Task Force recommended one-time HIV screening for all Americans aged 15 to 65.
What is the Window Period?

- HIV RNA (plasma)
- HIV p24 Ag
- HIV Ab

Eclipse Period
Acute Infection

Viral Detection
Antibody Detection
3rd generation EIA

Recent Infection
Longstanding Infection

Antibody Detection
2nd generation EIA
Antibody Detection
1st generation EIA

Seroconversion window
Schematic Version of Recommended Algorithm

4th generation HIV-1/2 immunoassay

(+)

(-)

Negative for: HIV-1 and HIV-2 antibodies and p24 Ag

HIV-1/HIV-2 antibody differentiation immunoassay

HIV-1 (+)
HIV-2 (-)

HIV-1 antibodies detected

HIV-1 (-)
HIV-2 (+)

HIV-2 antibodies detected

HIV-1 (+)
HIV-2 (+)

HIV antibodies detected*

HIV-1 (-) or indeterminate
HIV-2 (-)

HIV-1 RNA

RNA (+)
Acute HIV-1 infection

RNA (-)
Negative for HIV-1

*Additional testing required to rule out dual infection
Geenius™ HIV-1/2 Assay in the CDC Testing Algorithm

- HIV testing guidelines no longer recommend Western blot (WB) to confirm initial screening test
  - After reactive screen, perform HIV-1 versus HIV-2 differentiation assay

- Geenius HIV-1/2 assay (FDA approved 10/2014)
  - Automated reader and proprietary software to distinguish HIV-1 from HIV-2 reactivity

Multispot HIV Ab Test

• Supplemental test
  – used after a reactive 4th Gen EIA

• Replaces WB
  – More sensitive and specific than WB
  – Faster and less expensive than WB

• Will differentiate HIV-1 and HIV-2
Nucleic Acid Amplification Test for HIV-1 RNA

- Supplemental test
  - Used after a reactive EIA and a non-reactive Multispot
- Highly sensitive test which can detect the presence of viral RNA

- HIV-1 RNA/NAAT testing can detect acute HIV-1 infection
When should Antiretroviral therapy (ART) be initiated in individuals with HIV Disease?

A. CD4 count less than 200
B. CD4 count between 350 – 500
C. CD4 count greater than 500
D. Anytime
Panel’s Recommendations

- Antiretroviral therapy (ART) is recommended for all HIV-infected individuals. The strength of this recommendation varies on the basis of pretreatment CD4 cell count:
  - CD4 count <350 cells/mm³ (AI)
  - CD4 count 350 to 500 cells/mm³ (AII)
  - CD4 count >500 cells/mm³ (BIII)
- Regardless of CD4 count, initiation of ART is strongly recommended for individuals with the following conditions:
  - Pregnancy (AI) (see perinatal guidelines for more detailed discussion)
  - History of an AIDS-defining illness (AI)
  - HIV-associated nephropathy (HIVAN) (AII)
  - HIV/hepatitis B virus (HBV) coinfection (AII)
- Effective ART also has been shown to prevent transmission of HIV from an infected individual to a sexual partner; therefore, ART should be offered to patients who are at risk of transmitting HIV to sexual partners (AI [heterosexuals] or AIII [other transmission risk groups]; see text for discussion).
- Patients starting ART should be willing and able to commit to treatment and should understand the benefits and risks of therapy and the importance of adherence (AIII). Patients may choose to postpone therapy, and providers, on a case-by-case basis, may elect to defer therapy on the basis of clinical and/or psychosocial factors.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Recommendation to Initiate Therapy at CD4 count >500 cells/mm3

Growing awareness that untreated HIV may be associated with development of:

• Cardiovascular disease (CVD) and Kidney disease
• Liver disease
• Neurologic complications and Malignancy
• Availability of ART regimens that are more effective, more convenient, and better tolerated

Evidence from one observational cohort study that showed survival benefit in patients who started ART when their CD4 counts were >500 cells/mm3
Transmitted HIV Antiretroviral Drug Resistance (2007-2010)

10 HIV Surveillance Areas in US

- Any Class: Overall (n=18,144) 16.2%, Recent infection (n=3904) 17.9%, Long-standing infection (n=11,953) 15.5%
- NRTI: Overall (n=18,144) 6.7%, Recent infection (n=3904) 7.0%, Long-standing infection (n=11,953) 6.5%
- NNRTI: Overall (n=18,144) 8.1%, Recent infection (n=3904) 10.5%, Long-standing infection (n=11,953) 7.3%
- PI: Overall (n=18,144) 4.5%, Recent infection (n=3904) 4.5%, Long-standing infection (n=11,953) 4.1%

Total sample size: 77,887 newly diagnosed HIV-positive patients.
*P<0.01 versus long-standing infection.

Minority Species
Viral Infidelity

Honey please, just calm down. Let me explain....
Testing for Drug Resistance

• Before initiation of ART:
  – In absence of therapy, resistance mutations decline over time, but may persist and cause failure when ART is started
  – Resistance testing (genotype) recommended for all at entry to care

• Patients with virologic failure:
  – Perform while patient is taking ART, or ≤4 weeks after discontinuing therapy
  – Interpret in combination with history of ARV exposure and ARV adherence
Screening is recommended for HLA-B*5701 before starting patients on this HIV medication to reduce the risk of hypersensitivity reaction?

A. Abacavir  
B. Tenofovir  
C. Raltegravir  
D. Efavirenz  
E. Atazanavir
Assessment and Monitoring Studies

• HLA-B*5701 screening

  – Hypersensitivity reactions, generally occur during the first 6 weeks of treatment and include skin rashes, gastrointestinal symptoms, and respiratory symptoms

  – Recommended before starting ABC, to reduce risk of hypersensitivity reaction (HSR)

  – HLA-B*5701-positive patients should not receive ABC and positive status should be recorded as an ABC allergy
Treatment for ART Naïve Patients

NRTI/NTRTI
- Abacavir (ABC)
- Emtricitabine (FTC)
- Lamivudine (3TC)
- Tenofovir (TDF) NT
- Abacavir/Lamivudine
- Emtricitabine/Tenofovir

NNRTI
- Efavirenz (EFV)
- Rilpivirine (RPV)

Protease Inhibitors
- Atazanavir (ATV)
- Darunavir (DRV)
- Ritonavir (RTV)
- Darunavir/Cobicistat
- Atazanavir/Cobicistat

Integrate Inhibitor
- Raltegravir (RAL)
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- Dolutegravir (DTG)

Combinations
- Atripla
- Complera
- Stribild
- Triumeq

April 2015
www.aidsetc.org
New Developments

Tenofovir alafenamide (TAF, formerly GS-7340) “prodrug” of tenofovir (TDF) studies are ongoing:

• A 10-day monotherapy dosing study showed relative change in viral load

• TAF is stable in plasma and is predominantly hydrolyzed to TDF intracellularly resulting in higher intracellular levels and lower circulating levels of TDF

Ruane, PJ. J Acquir Immune Defic Syndr Volume 63, Number 4, August 1, 2013
Tenofovir Alafenamide (TAF) in a Single-Tablet Regimen in Initial HIV Therapy

Phase 3 (2 trials combined)

Treatment-naive
HIV RNA >1000 copies/mL
eGFR >50 mL/min

E/C/F: elvitegravir/cobicistat/emtricitabine + TDF or TAF
Non-inferiority margin: 12%
Baseline characteristics:
  Median age: 33-35 years, Male: 85%, Black race/ethnicity: 26%.
  Median HIV RNA: 4.5 log_{10} copies/mL.
  Median CD4 count: 405 cells/µL.

Wohl D, et al. 22nd CROI. Seattle, 2015. Abstract 113LB.
Results With TAF in a Single-Tablet Regimen in Initial HIV Therapy

- HIV RNA <50 copies/mL
  - TAF was non-inferior to TDF
    - Treatment difference: 2.0% (-0.7, 4.7)
  - High and similar response rates irrespective of baseline HIV RNA level, and baseline CD4 count
- Gain in CD4 count
  - Significantly greater increase with TAF versus TDF (211 versus 181 cells/μL; \( P=0.024 \))
- Treatment-emergent resistance <1% in both arms

Wohl D, et al. 22nd CROI. Seattle, 2015. Abstract 113LB.
Change in eGFR (Cockcroft-Gault) With TAF or TDF

- TAF versus TDF
  - Significantly smaller decreases in eGFR ($P<0.001$)
  - Significantly less proteinuria, albuminuria, and tubular proteinuria ($P<0.001$)
- No cases of Fanconi syndrome in either arm
- Discontinuations due to renal adverse events
  - E/C/F/TAF: 0 (0%)
  - E/C/F/TDF: 4 (0.5%)

Sax PE, et al. 22nd CROI. Seattle, 2015. Abstract 143LB.
• The FDA approved Triumeq based on the results from randomized controlled trials including: SINGLE, which tested the drug against Atripla (efavirenz/tenofovir/emtricitabine); SPRING-2, vs. Isentress (raltegravir); and FLAMINGO, vs. Prezista (ritonavir-boosted darunavir)
**Recommended Regimen Options**

(Drug classes and regimens within each class are arranged in alphabetical order.)

<table>
<thead>
<tr>
<th>INSTI-Based Regimens:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• DTG/ABC/3TC(^3) — only for patients who are HLA-B(^*)5701 negative (AI)</td>
</tr>
<tr>
<td>• DTG plus TDF/FTC(^3) (AI)</td>
</tr>
<tr>
<td>• EVG/c/TDF/FTC — only for patients with pre-treatment estimated CrCl ≥70 mL/min (AI)</td>
</tr>
<tr>
<td>• RAL plus TDF/FTC(^3) (AI)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PI-Based Regimens:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• DRV/r plus TDF/FTC(^3) (AI)</td>
</tr>
</tbody>
</table>

**Alternative Regimen Options**

(Drug classes and regimens within each class are arranged in alphabetical order.)

Regimens that are effective and tolerable, but that have potential disadvantages when compared with the recommended regimens listed above, have **limitations for use in certain patient population**, or have less supporting data from randomized clinical trials. **An alternative regimen may be the preferred regimen for some patients.**

<table>
<thead>
<tr>
<th>NNRTI-Based Regimens:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• EFV/TDF/FTC(^3) (BI)</td>
</tr>
<tr>
<td>• RPV/TDF/FTC(^3) — only for patients with pre-treatment HIV RNA &lt;100,000 copies/mL and CD4 cell count &gt;200 cells/mm(^3) (BI)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PI-Based Regimens:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• ATV/c plus TDF/FTC(^3) — only for patients with pre-treatment estimated CrCl ≥70 mL/min (BI)</td>
</tr>
<tr>
<td>• ATV/r plus TDF/FTC(^3) (BI)</td>
</tr>
<tr>
<td>• (DRV/c or DRV/r) plus ABC/3TC(^3) — only for patients who are HLA-B(^*)5701 negative (BIII for DRV/c and BII for DRV/r)</td>
</tr>
<tr>
<td>• DRV/c plus TDF/FTC(^3) — only for patients with pre-treatment estimated CrCl ≥70 mL/min (BII)</td>
</tr>
</tbody>
</table>
CD4 Count Monitoring

• CD4 monitoring for virologically suppressed patients whose CD4 counts have been consistently >500 cells/mm3 for at least 2 years should occur how often?

A. Every 3 months
B. Every 6 months
C. Every 9 months
D. Annually
E. Optional
Since 1991, CDC has investigated cases of HIV infection acquired by healthcare workers.

Confirmed cases (n=58)
- Nurses (41%), lab (35%), physicians (10%), other (14%)
- 1985 to 1998 (n=57)
  - Blood (n=49), concentrated virus (n=3), visibly bloody fluid (n=1), unspecified body fluids (n=4)
- 1999 to 2013 (n=1)
  - Lab technician sustaining needle puncture (2008)

Post Exposure Prophylaxis (PEP) is recommended for occupational exposures to HIV

The HIV status of the exposure source patient should be determined, if possible, to guide need for HIV PEP

PEP medication regimens should be started as soon as possible (2 hours) after exposure and should be continued for a 4-week duration
Risk of Infection

- Blood and visibly bloody body fluids

- Semen, vaginal secretions, cerebrospinal fluid, synovial fluid, pleural fluid, peritoneal fluid, pericardial fluid, and amniotic fluid

- Feces, nasal secretions, saliva, sputum, sweat, tears, urine, and vomitus are not considered potentially infectious unless they are visibly bloody
Exposure

• An exposure that might place HCP at risk for HIV infection is defined as a percutaneous injury

• Contact of mucous membrane or non-intact skin with blood, tissue, or other body fluids that are potentially infectious
Increased Risk

Exposure to a larger quantity of blood as indicated by:

(1) A device visibly contaminated with blood
(2) A procedure that involved a needle being placed directly in a vein or artery
(3) A deep injury
(4) Exposure to blood with a higher titer of HIV in blood
Selection of HIV PEP Regimen

• Favorable side effect profile and convenient dosing schedule, to facilitate adherence for 4 weeks

• PEP not justified for exposures that pose negligible risk of HIV transmission

• Consultation with experts is recommended, but should not delay PEP initiation
PEP Regimens

• Preferred HIV PEP regimen:

  – Raltegravir 400 mg BID + TDF/FTC (Truvada) Daily

  – Dolutegravir 50 mg + TDF/FTC (Truvada) Daily
PEP Regimens

• Alternative regimens (combine 1 drug or drug pair from left column with 1 NRTI pair from right column):

- Raltegravir
- Darunavir + ritonavir
- Etravirine +
- Rilpivirine
- Atazanavir + ritonavir
- Lopinavir/ritonavir
- Tenofovir + emtricitabine
- Tenofovir + lamivudine
- Zidovudine + lamivudine
- Zidovudine + emtricitabine

- Elvitegravir/cobicistat/tenofovir/emtricitabine (Stribild)
Summary of Recommendations:

• PEP medication regimens should contain 3 (or more) antiretroviral drugs

• Close follow-up for exposed personnel should be provided
  – counseling, baseline and follow-up HIV testing, and monitoring for drug toxicity and follow-up within 72 hours

• If a newer fourth-generation test is utilized for follow-up, HIV testing may be concluded 4 months after exposure otherwise HIV testing is typically concluded 6 months after an HIV exposure
PrEP & PEP
NEW WAYS TO PREVENT HIV
ACTION KIT FOR HEALTH CARE PROVIDERS
The use of antiretrovirals by HIV-uninfected persons before potential sexual is termed pre-exposure prophylaxis (PrEP).

The Food and Drug Administration (FDA) panel approved TDF-FTC for PrEP based on results of the iPrEx trial (42% reduction) and the Partners PrEP trial (75% reduction) in infections when compared to placebo.
PROUD Study: PrEP Use in a Real-World Setting (2012-2014)

Multicenter UK Study
13 Sexual Health Clinics

Open label
HIV-negative MSM
Condomless anal intercourse
No HBV

Follow-up: 3 times monthly for up to 24 months.
Primary endpoint: HIV infection in the first 12 months.
Baseline characteristics:
  Age: 35 years.
  White: 81%.
  No current relationship: 54%.
  Recreational drug use in the past 90 days: 70%.

PROUD Study: Results

- Significantly fewer new HIV infections with immediate versus deferred PrEP (3 versus 19 cases)
  - 86% reduction ($P=0.0002$)
  - Number needed to treat to prevent 1 infection: 13

- Preliminary analysis found that risk behaviors were similar between the 2 arms

PEP: post-exposure prophylaxis.

HIV for Primary Care

Friday, October 11, 2013
Cleveland Clinic Administrative Campus, 3050 Science Park Drive, Building 3
Beachwood, Ohio

TO REGISTER, VISIT ccfcmel.org/HIVPC

Did you know HIV patients have...
increased risk of cardiac disease?
elevated lipids?
higher risk for malignancies?
Changes in Causes of Death Over Time

- Individuals from D:A:D study followed from 1999 until death, loss-to-follow-up or February 2011

Death rate fell from 17.4 deaths per 1,000 in 1999-2000 to 8.3 deaths in 2009-2011
HIV and Aging

• In the U.S., approximately 30% of HIV-infected persons are ≥50 years of age and screening rates are low

• Reduced mucosal and immunologic defenses and changes in risk behaviors may lead to increased risk of HIV acquisition and transmission

• Older persons have decreased immune recovery and increased risk of non-AIDS events

• ART is recommended in patients >50 years of age, regardless of CD4 cell count (BIII)
HIV and the Older Patient: ART

• CD4 recovery on ART may be less robust in older patients (though virologic response appears to be the same as in younger patients)

• Starting ART at younger age may result in better outcomes (immunologic and perhaps clinical)

• Interactions between ARTs and other medications, as well as polypharmacy, may complicate care
## Comorbidities Associated with HIV and Aging

<table>
<thead>
<tr>
<th>Metabolic Issues</th>
<th>Organ-Related Issues</th>
<th>Neuropsychiatric Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin resistance</td>
<td>Liver disease</td>
<td>HIV-associated dementia</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Kidney disease</td>
<td>HIV encephalopathy</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>Peripheral vascular disease</td>
<td>Depression</td>
</tr>
<tr>
<td>Lipodystrophy</td>
<td>Cardiovascular disease/myocardial infarction</td>
<td>Mild neurocognitive impairment</td>
</tr>
<tr>
<td>Bone density loss</td>
<td>Cerebrovascular disease</td>
<td>Delirium</td>
</tr>
<tr>
<td>Mitochondrial toxicity</td>
<td>Osteopenia/osteoporosis</td>
<td>Depression</td>
</tr>
<tr>
<td>Chronic inflammation</td>
<td>Non-AIDS cancers</td>
<td>Anxiety</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Cancers caused by chronic infections</td>
<td></td>
</tr>
</tbody>
</table>

Barbour, S. and High, K., *IDSE, Volume 15, 2012*
Screening

• Fasting blood glucose (FBG) and/or hemoglobin A1c (HbA1c) should be obtained prior to and within 1–3 months after starting ART

• Patients with diabetes mellitus should have monitoring in accordance with the American Diabetes Association Guidelines

• Fasting lipid levels should be obtained prior to and within 1–3 months after starting ART
Screening

• Patients with abnormal lipid levels should be managed according to the National Cholesterol Education Program Guidelines

• Baseline bone densitometry (DXA) screening for osteoporosis in HIV-infected patients should be performed in postmenopausal women and men aged ≥50 years
HIV-Infected Women

• Abnormal cervical cytology is 10–11 times more common in HIV-infected women and is associated with the presence of HPV infection

• More frequent Pap tests should be considered in the following circumstances:
  – A previous history of an abnormal Pap
  – After treatment for cervical dysplasia
  – Symptomatic HIV infection
  – HPV infection
HIV-Infected Women

- HIV-infected women should have a cervical Pap test performed upon initiation of care, and repeated at 6 months and annually thereafter if results are normal.

- Women with atypical squamous cells, atypical glandular cells, low-high-grade SIL, or squamous carcinoma should undergo colposcopy and directed biopsy.

- MSM and women with a history of receptive anal intercourse or abnormal cervical Pap tests should have anal Pap tests.
HBV/HIV Coinfection and ART

• FTC, 3TC, and TDF are active against both HIV and HBV
  – Discontinuation may cause HBV flares

• HBV resistance to 3TC monotherapy
  – 40% at 2 years, 90% at 4 years
  – 3TC or FTC should be used in combination with other anti-HBV drugs

• Entecavir has activity against HIV; may select for M184V mutation, conferring cross-resistance to 3TC and FTC
  – Use only with fully suppressive ART regimen
The Path to a Cure

• “Functional cure” versus “Sterilizing Cure” is the ability to maintain undetectable viral loads without therapy

• Elite suppressors who control viral replication without therapy, are often considered examples of a functional cure

• ART cannot cure HIV infection due to the persistence of the virus in a small pool of latently infected and long-lived CD4-positive T cells

(Deeks and Walker, 2007)
Viral Reservoirs

- Reservoirs are infected cell populations that allow persistence of replication-competent HIV-1 in patients on optimal ART

- Several agents have been suggested to purge these reservoir cells

- Classes of small molecules capable of reactivating latent HIV-1 include histone deacetylase inhibitors such as vorinostat that induce transcription of HIV-1 through activation of the cellular protein kinase C pathway

  Archin et al., 2009; Contreras et al., 2009; Korin et al., 2002; Williams et al., 2004
The Berlin Patient

- His infection has been controlled without medications since 2008; after receipt of an allogeneic bone marrow transplant from a CCR5-deficient donor

- In a recent study samples of his blood and rectal biopsies were sent to various laboratories to detect any evidence of HIV, but the results were mixed

- “The meaning of these results will become clear only with longer follow-up, but in the meantime, we should maintain a balanced view”

  Daniel R. Kuritzkes, MD, Brigham and Women's Hospital
Websites to Access the Guidelines

• http://aidsinfo.nih.gov
• http://www.aidsetc.org